A CLINICO-EPIDEMIOLOGICAL STUDY OF HIV SEROCONCORDANT Vs SERODISCORDANT COUPLES

Dissertation Submitted in
fulfillment of the University regulations for

MD DEGREE IN
DERMATOLOGY, VENEREOLOGY AND LEPROSY
(BRANCH XII A)

MADRAS MEDICAL COLLEGE

THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY
CHENNAI
APRIL 2012

CERTIFICATE

Certified that this dissertation titled **"A CLINICO-EPIDEMIOLOGICAL STUDY OF HIV SEROCONCORDANT COUPLES Vs SERODISCORDANT COUPLES"** is a bonafide work done by **Dr. K.Radha Raja Prabha,** Post graduate student of the Department of Dermatology, Venereology and Leprosy, Madras Medical College, Chennai – 3, during the academic year 2009 – 2012. This work has not previously formed the basis for the award of any degree.

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SPECIAL ACKNOWLEDGEMENT

My sincere thanks to **Prof. Dr.V.Kanagasabai, M.D**., Dean, Madras Medical College for allowing me to do this dissertation and utilize the Institutional facilities.

ACKNOWLEDGEMENT

I am gratefully indebted to **Prof. Dr. V.Sudha, MD,DV,DD.,** Director and Professor, Institute of Venereology, for her invaluable guidance, motivation and help throughout the study. I would like to express my sincere and heartfelt gratitude to **Prof.Dr.S.Jayakumar, M.D.D.D,** Professor and Head of the Department, Department of Dermatology and Leprology for his guidance.

I express my sincere gratitude to **Dr. P.Elangovan MD,DV.,** Additional Professor, Institute of Venereology, for his invaluable guidance and support.

I express my sincere gratitude to **Dr.R.Arunadevi, MD.,DD.,** Head of the Department of Leprosy. I sincerely thank **Dr.C.Janaki, M.D.,D.D.,** Additional Professor of Dermatology (Mycology) for her priceless support. I am grateful to **Dr.V.Sampath, M.D.,** Additional Professor, Department of Dermatology for his invaluable guidance and help.

I express my earnest gratitude to **Dr.S.Nirmala, MD.DD.,** Professor and Head, Department of Occupational Dermatology and Contact Dermatitis for her constant motivation and guidance. I thank

Dr.R.Priyavathani Annie Malathy, MD,DD,DNB., Additional Professor, Department of Occupational Dermatology and Contact Dermatitis for her benevolent help and support.

I wish to thank **Dr.D.Prabhavathy, M.D.,D.D.**, Former Professor, Department of Dermatology, **Prof.Dr.S.V.Somasundaram MD.,** Former Professor, Department of Occupational Dermatology ,**Dr.K.Gajendran, M.D.,D.V.**, Former Director, Institute of Venereology for their constant support and motivation.

I humbly thank my Co-Guide **Dr.P.Prabahar, M.D(DVL).,** for his valuable guidance throughout my work.

I am inclined to thank **Dr.V.Thirunavukarasu, M.D.,D.V**., **Dr.K.Venkateswaran, M.D.,D.V.**, **Dr.P.Mohan, M.D.,D.V.**, **Dr. S. Thilagavathy M.D.,D.V., Dr.S.Arunkumar M.D.,D.V**., **Dr.S.Kalaivani, M.D.,D.V, Dr. Ahamed Shariff MD(DVL) ., Dr. Uma Maheshwari, M.D(DVL)., Dr.Sowmiya,M.D (DVL)** and **Dr C.Vidhya, MD(DVL).,** Assistant Professors, Department of Venereology, for their help and suggestions.

My sincere thanks go to **Dr.S.Kumaravel M.D,D.D.**, **Dr. G.K. Tharini M.D., Dr.J. Manjula M.D, DNB**., **Dr. C. Vijayabhaskar MD, Dch., Dr. S.J. Daniel MD(DVL),**

Dr.Madhu MD, DCH., Dr.S.Anupama Roshan, D.D.V.L., and **Dr.N.Hema, M.D,** Assistant professors, Department of Dermatology for their kind support and encouragement.

I thank, **Dr. A. Hameedullah, M.D.D.D., Dr.Afthab Jameela Wahab M.D,D.D**., **Dr.N.Saravanan, MD(DVL), Dch.,** Assistant Professors, Department of Occupational Dermatology and Contact Dermatitis for their support and help.

I wish to thank and give homage to our beloved Former Additional Professor **Late Dr.N.Kumar M.D, D.V, D.M.R.D.,** and **Late Dr.V.Thirunavukarasu M.D, D.D.,** for their moral support.

I would like to express my immense gratitude to the **patients** and their families without their participation this study would not be happened.

Last but not least words are inadequate to express my gratitude to my husband, **Dr.A.Sathish Selva Kumar** his unrelenting support, patience and friendly attitude enabled me to complete this work.

Constraint of space may have led to few names gone missing in my acknowledgement. I wish to express sincere gratitude to all those who have been associated with my study and have helped me in bringing this dissertation to the present form.

CONTENTS

Introduction

The HIV epidemic of India arouses a great epidemiological interest. India accounts for roughly half of Asia's HIV prevalence and has the third largest number of people living with HIV/AIDS [1]. Although HIV prevalence is high among sex workers and drug users, clients of sex workers are the most powerful driving force in India's HIV epidemics and constitute the largest infected population group in the country. As per National behavioural surveillance survey in 2006, 2.4 percent of adult males i.e., around 73.5 lakh adult males have visited commercial sex workers during the year prior to the survey. These men then transmit the infection to their wives and they form transmission bridge from the high risk group to the general population.

According to 2010 report of the Joint United Nations Program on HIV/AIDS (UNAIDS), more than 90 percent of infected women have acquired the virus from their husbands or intimate partners.[1] In most cases, women are at an increased risk not due to their own sexual behaviour, but because their partner is an IDU or also has FSWs or MSM as other sex partners[2]. The factors that are likely to influence HIV transmission among married couples are poorly studied and need to be clearly established. Based on the serological status couples can be

Seroconcordant couple

Both partner are on same HIV status either they are HIV positive or negative

Serodiscordant couple

Couple in which one partner is HIV positive other is HIV negative, having different serostatus

HIV negative individuals in discordant partnerships are at a high risk of acquiring infection and preventive interventions targeted at such individuals are urgently needed. This study is carried out to assess the prevalence of HIV among such low risk women and to identify the risk factors that favor HIV transmission among married couples, so that serodiscordance can be identified and counselled accordingly.

Review of Literature

Introduction

It is now 25 years since acquired immune deficiency syndrome (AIDS) was first recognized as a novel disease. Within 2 years of defining AIDS as a distinctive syndrome in 1981, the human immunodeficiency virus (HIV) was identified as the causative agent. HIV infection is acquired sexually, from blood or blood products, or vertically from an infected mother during pregnancy, birth or breastfeeding. The virus infects immunocompetent cells including CD4 T cells and macrophages. It creates variable patterns of disease in individuals, groups and races but all are characterized by evolving, sometimes fulminant immunodysfunction (AIDS) affecting many systems of the body.

HIV IN INDIA

HIV epidemic has been evolving in the country since the first case was detected in Tamil Nadu in 1986[4]. In 2009 the National AIDS Control Organization (NACO) of the government of India has estimated that around 2.4 million people were living with HIV with a prevalence of 0.3%.[3] Of these, an estimated 39% are female and 3.5% are children.[3]

According to the 2010 UNGASS HIV country report, India's epidemic is concentrated within most-at-risk-populations (MARPs), with prevalence substantially higher among these populations than in the general population. Prevalence also varies dramatically by district, state, and region, with

numerous isolated pockets of high prevalence. Approximately 60 percent of people living with HIV/AIDS (PLWHA) live in the six high-prevalence states. The high prevalence states includes Andhra Pradesh, Tamil Nadu, and Maharashtra and in the North eastern states of Nagaland and Manipur.

WAVES OF HIV EPIDEMIC

HIV epidemics spread classically in 3 waves.[5]

- The first wave is seen amongst the sex workers and the IDUs who form the core transmitters or the **core groups**.
- The second wave reaches the clients of the core transmitters group. The HIV infection is brought to the low risk population from the core transmitters group through the **bridge population**. The bridge population is used to connote the mobile population such as truck drivers, single male migrants etc.
- When the spouses, children and relatives of the clients of sex workers get affected the third wave is completed.
- Recently a fourth wave constituted by the adolescents has also been proposed.

HIV VIROLOGY

Human immunodeficiency virus (HIV)

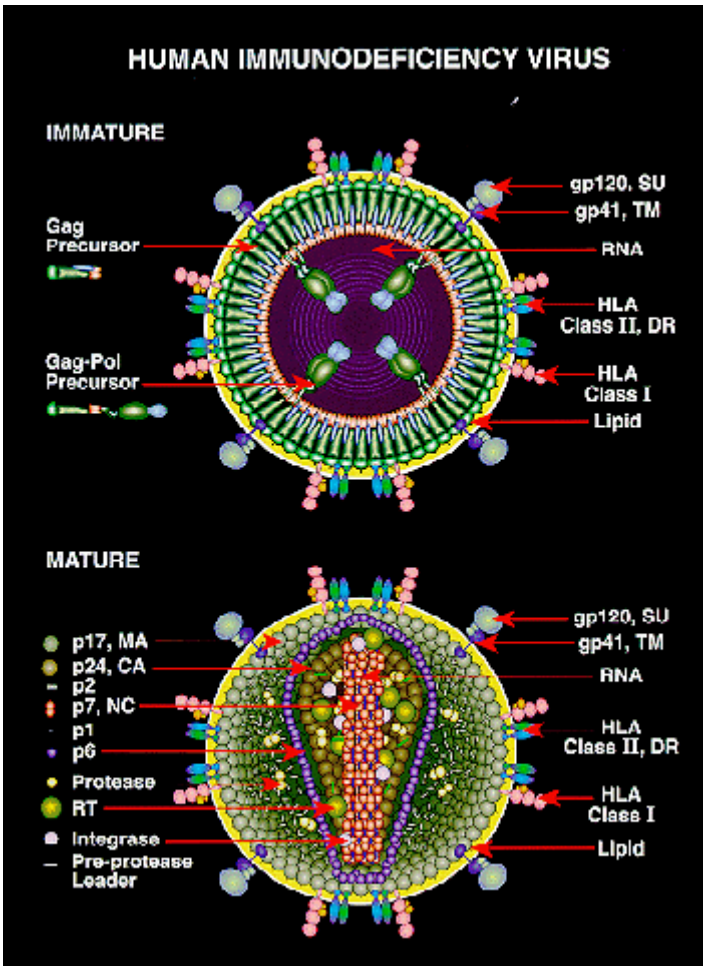
HIV is a retrovirus belonging to the subfamily of lentivirus. There are two main types of HIV: HIV1 and HIV 2. HIV 1 and 2 have originated from the Simian immunodeficiency virus (SIV) probably from the once found in chimpanzees (SIVcpz) and in sooty mangabey monkeys (SIVsm). HIV is a lymphocytotropic and neutrotrophic virus. Therefore it may be found in almost all the body fluids and organs. It is present in infective discharges in semen, vaginal, cervical secretions and blood.

HIV-1 contains a single-stranded RNA genome that is 9 kilobases in length and contains 9 genes that encode 15 different proteins.[6] The major viral proteins (some of which contain >1 protein subunit) are classified as structural proteins (Gag, Pol, and Env), regulatory proteins (Tat and Rev), and accessory proteins (Vpu, Vpr, Vif, and Nef).[7]

Differences between HIV1 and HIV2[8]

Character	**HIV1**	**HIV2**
Prevalence	Globally	Africa
Virulence	Highly infective	Less infective
Mother to child transmission	High(24.7%)	Low(1.2%)
Incubation period	Shorter compared to HIV2	longer

Structure of HIV virus



HIV-1 subtypes

Three major classes of HIV-1 have emerged: M (major), N (new), and O (outlier). Among M group viruses, which account for >90% of HIV infections worldwide, there are 9 subtypes, called clades, designated by the letters A-D, F-H, J, and K, as well as many recombinant form[9][10]. Variation between one clade and another in the amino acid sequences of the envelope protein may exceed 30%. As seen in the map the viral diversity is greatest in sub-Saharan Africa.

Due to the increased occurrence of mutations in the viral population an infected individual is likely to have swarm virus variants (Quasi species). According to phylogenetic studies most of the HIV1 strains belong to subtype C in India. The predominant HIV1 subtype in US and Europe is subtype B whereas HIV E and B are common in Thailand. A new recombinant HIV between C and A has been reported from Pune.[11]

Pathogenesis

Entry to the cell

HIV enters macrophages and $CD4^+$ T cells by the adsorption of glycoproteins gp160 on its surface to receptors (either CCR5 or CXCR4) on the target cell followed by fusion of the viral envelope with the cell membrane and the release of the HIV capsid into the cell.[12][13] gp120 binds to integrin $\alpha_4\beta_7$ activating LFA-1 the central integrin involved in the establishment of virological synapses, which facilitate efficient cell-to-cell spreading of HIV-1.

Viral replication

Shortly after the viral capsid enters the cell, an enzyme called reverse transcriptase liberates the single-stranded (+)RNA genome which copies it into a complementary DNA (cDNA) molecule.[14]The process of reverse transcription is extremely error-prone, and the resulting mutations may cause drug resistance or allow the virus to evade the body's immune system. The

reverse transcriptase also has ribonuclease activity as well as DNA-dependent DNA polymerase activity.[15] Newly synthesised complement form a double-stranded viral DNA that is then transported into the cell nucleus. The integration of the viral DNA into the host cell's genome is carried out by another viral enzyme called integrase

Viral assembly and release

The final step of the viral cycle, assembly of new HIV-1 virons, the env polyprotein (gp160) goes through the endoplasmic reticulum where it is cleaved by protease and processed into the two HIV envelope glycoproteins gp41 and gp120[16]. These are transported to the plasma membrane of the host cell where gp41 anchors the gp120 to the membrane of the infected cell. The Gag (p55) and Gag-Pol (p160) polyproteins also associate with the inner surface of the plasma membrane along with the HIV genomic RNA as the forming virion begins to bud from the host cell. During maturation, HIV proteases cleave the polyproteins into individual functional HIV proteins and enzymes. The various structural components then assemble to produce a mature HIV virion. The mature virus is then able to infect another cell

ROUTES OF TRANSMISSION

Sexual route

The primary method of spread of HIV infection worldwide is through sexual exposure. In the areas of highest HIV prevalence globally,

heterosexual intercourse is the primary mode of transmission, accounting for approximately 70% of the overall sexual transmission.[17] In the United States and Europe, acquisition of the virus through homosexual contact remains important, and there is some evidence of increasing incidence of infection among young gay men and ethnic minorities.[18]

HIV has been isolated from blood, seminal fluid, pre-ejaculate, vaginal secretions, cerebrospinal fluid, saliva, tears, and breast milk of infected individuals.[19][20]In genital fluids, HIV may be found in both cell-free and cell-associated compartments, but it is unknown which is responsible for productive infection.[21] Viral concentrations in tears and saliva are comparatively low, and there are substances in saliva that appear to inhibit infectivity. No cases of HIV infection have been documented to arise from contact with non-bloody saliva or tears. Female-to-female HIV transmission has been reported, but is rare.[22] Serum HIV viral load is strongly associated with heterosexual transmission between HIV-serodiscordant African sexual partners, where transmission was noted to be rare at viral loads <1,500 copies/ml.[23]

Nonsexual HIV transmission

Nonsexual HIV transmission can occur through transfusion with contaminated blood products, injection drug use, occupational exposure, or accidental needle sticks. The risk from occupational needle sticks to health care workers from known HIV-positive source patients in case series

performed prior to the availability of potent ART was found to be 0.33-0.5%.[24] Factors increasing the risk of HIV acquisition from an occupational needle stick include deep injury, injury with a visibly bloody device, or injury with a device that had been previously used in the source patient's vein or artery.[25]

Mother to child transmission (MTCT)

The risk of transmission of HIV from pregnant mother to child is between 21 and 43% in developing countries.[26] The transmission of the virus from the mother to the child can occur in utero (during pregnancy), intrapartum (at childbirth), or via breast feeding[27]

	In utero	**Intrapartum**	**Breast feeding**
% of mother to child transmission	10 to 15%	50 to 70%	10to 15%

In a study conducted in Malawi the HIV incidence in breastfed infants between 1 and 5 months is higher (0.7% per month) when compared to that between 6 and 11 months (0.6% per month) and 12 and 17 months (0.3% per month)[28]. However now it is shown that exclusive breast feeding is better than mixed feeding.[29]

Interplay of Factors Driving Sexual Transmission

Duration of infectiousness

Lack of cure and long duration of infectiousness are the characteristics of HIV that distinguishes it from other STIs. The long asymptomatic period associated with HIV infection puts many of the contacts at higher risk of acquiring the infection.

Risk of infection per contact

The average risk of acquiring HIV infection per exposure through various route is given below. Among sexual exposure, Anal sex caries the highest risk, especially for the receptive partner.

Exposure Route	**Estimated infections per 10,000 exposures to an infected source**
Blood transfusion	9,000 (90%)[31]
Mother-to-child, including pregnancy, childbirth and breastfeeding (without treatment)	2,500 (25%)[32]
Mother-to-child, including pregnancy, childbirth and breastfeeding (with optimal treatment)	100–200 (1%–2%)[32]
Needle-sharing injection drug use	67 (0.67%)[33]
Percutaneous needle stick	30 (0.30%)[34]
Receptive anal intercourse (2009 and 2010 studies)	[30–890][35] 143 [48–285][30]

Insertive anal intercourse for uncircumcised men (2010 study)	62 (0.62%)[7–168][30]
Insertive anal intercourse for circumcised men (2010 study)	11 (0.11%) [2–24][30]
Low-income country female-to-male	38 (0.38%) [13–110][35]
Low-income country male-to-female	30 (0.3%) [14–63][35]
Receptive (female) penile-vaginal intercourse	10 (0.1%)[36][37]
Insertive (male) penile-vaginal intercourse	5 (0.05%)[36][37]
Fellating a man	1 (0.01%)[37]
Man being fellated	0.5 (0.005%)[37]

The per contact risk of HIV transmission with a commercial or a casual partner is likely to be less than for other STDs example gonorrhoea. The risk of infection per contact is not the same every time and it depends on the following:[5]

- Concordance of the HIV status among the couples
- Stage of HIV infection
- Untreated associated STIs
- Use of barrier methods
- Male circumcision
- Sexual behaviours and practices

Behavioural and social factors [5]

- little or no condom use
- large number of adult population with multiple sex partners

- large sexual networks—people moving back and forth between home and place of work
- age mixing typically between old men and young women
- Women's economic dependence robs them of their control over their right to have safer sex.

Biological factors

- High rates of STIs especially those causing genital ulceration and low rates of male circumcision
- High viral loads- high levels during the initial infected stage and again during the later stages

Bridge population

The bridge population is constituted by those who have sex with both high risk and low risk partners. The bridge behaviour involves transmission of HIV across sub-population having different risk behaviours. Studies have shown that MSMs having sex with both commercial and non commercial sex partners play a major role in the transmission of HIV. [5]

Vulnerability of women to HIV

Women are biologically more susceptible than men to HIV infection. Male to female transmission is 2-4 times more efficient than female to male transmission and this is because [5]

- Females have larger mucosal surface exposed during sexual intercourse.
- Another reason is that of higher concentration of HIV in semen than in vaginal fluids.[42]
- Many STIs in women are asymptomatic than men, so there is delay in seeking medical help
- Stigma of attending an STI clinic is more attached with women than in men.
- Women are also exposed to the risk of blood products transfusion due to their childbearing role.
- women's inability to negotiate safe sex practises with their partners make women more vulnerable to HIV infection.
- Men's unwillingness to use condoms further accentuates women's risk. In a study of the prevalence of and risk factors for HIV infections in TamilNadu (1994-1995) only 2% of married men were found to use condoms.[5]

Socioeconomic consequences

People with lower literacy and from poor families have higher risk of HIV.[43] For people already living in poverty, further income loss can threaten their ability to meet basic needs such as food.[44] Poverty also forces people to accept choices that put them at risk for HIV infection. Studies reveal that poor women are forced into sex work and into providing sexual favors in return for money, and to be less able to insist on condom use. [45]

Role of condoms in transmission of HIV

According to the Centers for Disease Control & Prevention (CDC), a number of carefully conducted studies, employing rigorous methods and measures, have demonstrated that consistent condom use is highly effective in preventing HIV transmission.[38][39]

- In a two-year study of serodiscordant couples no uninfected partner became infected among couples using condoms correctly and consistently at every act of vaginal or anal sex versus 10 percent of those using condoms inconsistently.[38][40]
- In a similar two-year study, two percent of uninfected partners who used condoms consistently became HIV-infected versus 12 percent among those who used condoms inconsistently or not at all.[38]
- Increased use of condoms in casual relationships is important in Uganda's declining HIV infection rates.[41]

Male circumcision and HIV

Male circumcision is defined as the surgical removal of all or part of the foreskin of the penis and may be practiced as part of a religious ritual, as a medical procedure, or as part of a traditional ritual performed as an initiation into manhood. There is strong evidence that medical male circumcision reduces the acquisition of HIV by heterosexual men by between 38% and 66% over 24 months. Inclusion of male circumcision into current HIV prevention measures guidelines is warranted by the UNAIDS and the WHO in

2007.[46] Researchers have noted that the inner aspect of the foreskin is well supplied with Langerhans cells and that in vitro, HIV-1 demonstrates a specific tropism for these cells, in particular the CD4 receptors on them. According to this theory, circumcision would remove the potential entry site for HIV; however, in direct contradiction to the above theory, the inner prepuce contains apocrine glands which secrete lysozyme. Lysozyme reportedly kills HIV-1 in vitro, suggesting a protective effect of the foreskin. [46]

CLASSIFICATION OF HIV DISEASE

HIV damages the immune system, leaving the infected person vulnerable to a variety of infections called "opportunistic" infections. The effect of HIV on the immune system is monitored by measuring the CD4 (helper) lymphocyte count in the blood. A normal CD4 count is approximately between 600 and 1,200 cells/μL. CD4 counts <500 cells/μL indicate that impairment of immune function is present, and are an indication for ART. CD4 counts <200 cells/μL indicate imminent risk of serious OIs or other complications of HIV disease, and prompt treatment is recommended.[47]

The World Health Organization has developed a clinical staging system for HIV infection.[48]This system relies more heavily on clinical rather than laboratory evaluation, and has been used widely in resource-constrained areas where laboratory testing is not widely available.

Table 3: WHO Staging System for HIV Infection and Disease in Adults and Adolescents (a)

Clinical stage I

1. Asymptomatic
2. Persistent generalized lymphadenopathy

Performance scale 1: asymptomatic, normal activity

Clinical stage II

1. Weight loss, <10% of body weight
2. Minor mucocutaneous manifestations (seborrheic dermatitis, prurigo, fungal nail infections, recurrent oral ulcerations, angular cheilitis)
3. Herpes zoster within the last 5 years
4. Recurrent upper respiratory tract infections (i.e., bacterial sinusitis)

And/or performance scale 2: symptomatic, normal activity

Clinical stage III

1. Weight loss, >10% of body weight
2. Unexplained chronic diarrhoea, >1 month
3. Unexplained prolonged fever (intermittent or constant), >1 month
4. Oral candidiasis (thrush)
5. Oral hairy leukoplakia
6. Pulmonary tuberculosis within the past year
7. Severe bacterial infections (i.e., pneumonia, pyomyositis)

And/or performance scale 3: bedridden <50% of the day during the last month

Clinical stage IV

1. HIV wasting syndrome, as defined by the U.S. Centers for Disease Control and Prevention (CDC)
2. Pneumocystis jiroveci (formerly carinii) pneumonia
3. Toxoplasmosis of the brain
4. Cryptosporidiosis with diarrhoea >1 month

5. Cryptococcosis, extrapulmonary
6. Cytomegalovirus disease of an organ other than liver, spleen, or lymph nodes
7. Herpes simplex virus infection, mucocutaneous >1 month, or visceral any duration
8. Progressive multifocal leukoencephalopathy
9. Any disseminated endemic mycosis (ie, histoplasmosis, coccidioidomycosis)
10. Candidiasis of the oesophagus, trachea, bronchi, or lungs
11. Atypical mycobacteriosis, disseminated
12. Nontyphoid Salmonella septicemia
13. Extrapulmonary tuberculosis
14. Lymphoma
15. Kaposi sarcoma
16. HIV encephalopathy, as defined by the CDC

    And/or performance scale 4: bedridden >50% of the day during the last month

NATURAL HISTORY OF UNTREATED HIV INFECTION

Acute retroviral syndrome

The acute viral syndrome of primary HIV infection (sometimes referred to as "seroconversion illness") was first defined in 1985, with symptoms resembling those of mononucleosis appearing within 2 to 4 weeks following exposure to HIV.[49][50] The most common presenting symptom is fever, seen in over 75% of patients.[51] Other common symptoms include lymphadenopathy, headache, rash, joint pains, night sweats, and mucosal candidiasis and pharyngitis.[52] The neurological features include

meningoencephalitis, peripheral neuropathy, facial palsy, Guillian-Barre syndrome, cognitive impairment and psychosis. The non-specific symptoms of primary HIV infection may make diagnosis a challenge and therefore requires a high index of clinical suspicion. Routine HIV antibody testing may be negative for several weeks or even months after exposure in the so-called "window period.".[53]

During primary infection with HIV, plasma viral load often reaches very high levels in the range of millions of RNA copies/mL. [54][55] Thus, for individuals in whom primary HIV infection is clinically suspected, HIV RNA assays, which have a sensitivity approaching 100% and specificity of 97.4% in this setting, and positive RNA tests during acute infection should be confirmed by documentation of subsequent HIV antibody conversion.[56]

Aggressive ART during acute retroviral illness protects activated HIV specific CD4 cells from HIV infection to preserve a response analogous to the response seen in non-progressors. [57]

Asymptomatic HIV infection

After the period of acute HIV infection during which CD4 counts and viral load change dramatically and a relative equilibrium between viral replication and the host immune response is reached, and individuals may have little or no clinical manifestations of HIV infection except persistent generalised lymphadenopathy (PGL). PGL is defined as enlarged lymph

nodes (>1cm) involving at least two non contiguous site, other than inguinal nodes, in absence of an obvious cause.[58] This time between initial infection and the development of AIDS may be long, averaging 10 years, even in the absence of treatment.[59]

Symptomatic HIV disease

During the relative clinical latency the viral replication and the CD4 count turnover remains active with most affected individuals having a disease progression due to the increased loss of CD4 cell counts (by 50-90 cells/μL per year in asymptomatic individuals) and a perturbation of the host immune system.[60][61] The rate of progression of infection may vary considerably.

During early symptomatic HIV infection, the skin and mucous membranes are predominantly involved. Constitutional symptoms include unexplained fever, weight loss, recurrent diarrhoea, fatigue and malaise. Widespread seborrheic dermatitis, folliculitis, recurrent herpes simplex infection, oral candidiasis, oral hairy leukoplakia and herpes zoster are most common presentation.

Late symptomatic stage is characterised by risk of developing opportunistic infections. Common conditions are Pneumocystis carinii pneumonia, toxoplasmosis, disseminated Mycobacterium avium complex infection, oesophageal candidiasis and related malignancies.

Clinical AIDS

According to CDC criteria, AIDS is defined by either diagnosis of one of the AIDS-defining conditions, or by measurement of CD4 levels <200 cells/μL. This stage is characterised by AIDS defining infections and malignancies. Some of more frequently seen infections are CMV, cryptococcal meningitis, histoplasmosis and cervical dysplasia. CNS involvement is very prominent: AIDS dementia, CNS lymphoma and CMV infections. Survival time from the development of AIDS varies according to the AIDS-defining event. The mean survival time after diagnosis of AIDS in the United States prior to the availability of antiretroviral treatment was 10-12 months.[62]

Long-term non progressors(LTNPs)

A small subset of individuals infected with HIV--probably <5%--remain free of symptoms, achieve good control of HIV viral replication, and maintain high CD4 counts in the absence of antiretroviral medications over many years of infection, (98) In general, LTNPs appear to have strong cellular immune responses to a variety of HIV antigens.[64][65]

INTERACTION BETWEEN HIV AND STIs

The complex interaction between STIs and HIV has been demonstrated in many epidemiological, in vitro and clinical studies over the last many

years. STDs could facilitate HIV 1 transmission by increasing the infectiousness of the index case, the susceptibility of the partner or both.

STIs As a cofactor for HIV transmission

Both ulcerative and non-ulcerative STIs promote HIV transmission by augmenting HIV infectiousness and HIV susceptibility via different biological mechanisms.

Effect of ulcerative STIs on HIV transmission

Lack of mechanical skin or mucous membrane barrier makes easy viral entry due to ulcertation or microulceration.[66]

Sexually transmitted infection which usually present as genital ulceration includes

Syphilis (Treponema pallidum)

Chancroid (Haemophilus ducreyi)

Granuloma inguinale (klebsiella granulomatis)

Lymphogranuloma venerum (Chlamydia trachomatis)

Genital herpes (Herpes simplex virus)

Method by which genital ulcer diseases favors HIV transmission

- Among HIV-seronegative individuals, genital ulcers may increase the susceptibility to HIV by disrupting mucosal and skin integrity
- Increasing the presence and activation of HIV susceptible cells in genital tract (the susceptibility cofactor effect).[67]

- Haemophilus ducreyi, for example, evokes a cell-mediated immune response which attracts HIV susceptible cells to the ulcer surface. In fact, H.ducreyi may contain specific T cell-stimulating antigens which further predispose T cells to infection by HIV.[67]
- viral STDs such as herpes interact in the genital tract, which promotes the establishment of HIV infection. For example, in tissues coinfected with HSV-1, the virions are able to infect keratinocytes despite the lack of CD4 receptors. In gaining access to the cells, HIV may also take advantage of changes in cellular chemokine receptors that had resulted from infection with other viruses, as shown in recent studies of cytomegalovirus.[67]
- Genital ulcers bleed frequently during sexual intercourse, resulting in a potential-increase in HIV infectiousness (the infectivity cofactor effect).
- The presence of HIV in genital ulcer exudates in HIV infected individuals confirmed by culture and PCR (the infectivity cofactor effect).[68]
- Increased number of HIV-containing white blood cells in both ulcerative and inflammatory genital secretions (the infectivity cofactor effect).
- Increasing HIV replication by certain ulcerative STD pathogens (e.g.Treponema pallidum lipoproteins) and increasing the number of receptors expressed pp-cell receptive to HIV 1 (e.g. H. ducreyi lipo-

oligosaccharide may increase the CCR5 receptors on a macrophage cell line)[67]

Effect of urethritis on HIV transmission

Urethritis is defined as infection-induced inflammation of the urethra. STD causes of urethritis are categorized as either

- gonococcal urethritis (ie, due to infections with Neisseria gonorrhoeae)
- NGU (ie, due to infections with following organism)
    - Chlamydia trachomatis,
    - Ureaplasma urealyticum,
    - Mycoplasma hominis, Mycoplasma genitalium,
    - Trichomonas vaginalis

Rare infectious causes of urethritis include

- lymphogranuloma venereum, herpes genitalis, syphilis, streptococcal, staphylococci and anaerobes.

  causes increased shedding of HIV virus in the genital tract (the infectivity cofactor effect), probably by recruiting HIV infected inflammatory cells as part of the normal host response. Investigators have noted a significant increase in the detection of HIV 1 DNA in cervicovaginal fluids of patients with gonorrhoea and chlamydial infection.[69]

Association between STDs and HIV Infection[67]

STDs	**Increased Risk for HIV Acquisition**		**Clinical exacerbation**
N+ gonorrhoeae infection	+/-	3 to 5 times	+/-
Chlamydial infection	+	3 to 5 times	+/-
Trichomonas vaginalis infection	+	3 to 5 times	-
Bacterial vaginosis	+	2 to 5 times	-
Chancroid	+	2 to 5 times	+
Syphilis	+	3 to 9 times	+
Genital herpes	+	2 times	+
Granuloma inguinale	+	+/-	
Human Papilloma infection	+	+	
LGV	+	+/-	
Hepatitis B	-	+	

Role of cervicitis in HIV transmission

Sexually transmitted diseases (STDs) that can cause cervicitis include:

- Chlamydia
- Gonorrhea
- Herpes virus (genital herpes)
- Human papilloma virus (genital warts)
- Trichomoniasis

For cervicitis specifically, three potential mechanisms have been suggested to explain the observed relationship of cervicitis and HIV infection.

a. Recruitment of inflammatory cells to the cervical mucosa may result in increase concentration of HIV infected CD4 lymphocytes-macrophages.

b. In the presence of an inflammatory milieu, HIV replication is enhanced, perhaps through the generation of reactive oxygen products secreted by granulocytes and secondary to cell activation which is mediated by inflammatory cytokines (interleukin-1 or tumour necrosis factor alpha).[67]

c. Cervicitis is associated with micro-ulceration and friable mucosal tissue that provides a portal of exit or entry for virus or infected cells.

Bacterial vaginosis and HIV transmission

Bacterial vaginosis (BV) is polymicrobial syndrome involving the replacement of normal vaginal flora lactobacilli by a wide variety of the anaerobic bacteria and mycoplasmas. It requires a special mention since it is a common vaginal infection in women, and the relative risk of transmission of HIV is 2 to 5 times in the presence of BV. Schmid et al have summarized all possible mechanisms from research studies of different workers:[67]

- Lactobacilli produce lactic acid that maintains vaginal pH and inhibits the growth of many organisms, including those associated with BV. Some lactobacilli particularly those posted against the development of

BV produce hydrogen peroxide which is toxic to a number of organisms including HIV.[70]

- Low vaginal pH may inhibit CD4 lymphocyte activation and, therefore, decrease HIV target cells in the vagina. Therefore, a high vaginal pH due to the presence of BV may make the vagina more conducive to HIV survival and adherence.[70]
- BV has also been shown to increase the intravaginal levels of interleukin-10, which increases the susceptibility macrophages to HIV.
- A heat-stable protein elaborated by Gardnerella vaginalis increase production of HIV by as much as 77 fold.[67]
- Mycoplasma hominis is the potent inducer of HIV 1 expression among several vaginal bacterial species studied.[67]

Role of Trichomonas vaginalis in HIV transmission

Trichomonas may amplify HIV-1 transmission by increasing susceptibility in an HIV-1-negative person and the infectiousness in an HIV-1-positive patient. The biological rationale for this is compelling:

- The natural history of this organism, including its often symptomless nature and protracted carriage, may also contribute to increasing HIV-1 transmission.
- T. vaginalis isolates are cytotoxic to urogenital epithelial cells.[71]

- The organism typically elicits an aggressive local cellular immune response, with heavy infiltration of leucocytes, even in symptom-free patients.
- About 50% of infected women have punctate haemorrhages which can be observed on colposcopy.[72]

Thus in an HIV-1-negative person, it can enlarge the portal of entry for HIV-1 by increasing the number of HIV-1 target cells available and viral access to the bloodstream. In an HIV-1-infected patient, the leucocyte infiltration and haemorrhages induced by trichomonas may expand the portal of exit and increase shedding of HIV-1 in the genital area. [73]

Effect of genital candidiasis on HIV transmission

C. albicans causes vaginal inflammation that may compromise the integrity of the vaginal mucosa. Vaginal inflammation usually results after Candida hyphae overcome the normal bacterial vaginal flora and invade the epithelium. The body responds by recruiting polymorphonuclear leukocytes to kill Candida. [74]

Presence of vulvovaginal candidiasis is associated with an increase in the number of copies of cell-associated and cell-free HIV-1 RNA in women who are seropositive for HIV. [75]

Role of HPV on HIV transmission

Human papillomavirus (HPV) infection, one of the very common STIs, presents as genital warts to carcinoma in HIV-positive patients.

- The local immune response elicited by HPV infection predisposes to HIV acquisition, and that individual in the process of clearing an HPV infection might be at increased risk. Thus risk of acquiring infection increase with the increasing numbers of concurrent HPV infections, and HPV infections clearance.[76]
- Enhanced friability and inflammation of the cervix from HPV disease or infection
- The anal lesions caused by HPV bring blood vessels closer to the surface in the anus and make the lining of the anus thinner and more fragile.[77]

Effects of STD management on HIV Transmission

In a study conducted in Malawi the results showed that HIV 1 positive men with urethritis had eight times higher HIV-1 concentrations in seminal plasma than that in seropostive men without urethritis. After treatment, the concentration of HIV 1 RNA in semen decreased significantly. Ghys and co-workers found a significant increase of HIV 1 DNA in Cervicovaginal lavage samples from patients with gonorrhoea Chlamydia infection, Cervicovaginal ulcer or cervical mucopus. A week after STI treatment, the detection of HIV 1

in these secretions decreased from 42 to 21%; however changes in detection rate were not observed in women whose STIs were not cured. [67]

A compelling body of evidence shows that prevention, early diagnosis and treatment of STDs can be important in a HIV prevention strategy. This is particularly true when treatment of symptomatic STIs is addressed.

LABORATORY TESTING OF HIV

HIV antibody testing

HIV infection is usually diagnosed by testing serum for antibodies to HIV using a commercially available enzyme-linked immunosorbent assay (ELISA or EIA). Because the ELISA test is not entirely specific, positive results are confirmed with a Western blot assay, which identifies antibodies to specific components of HIV.[78][79] An infected individual may test ELISA negative during a "window period" that varies in length from a few weeks to a few months after infection. Newer methodologies allow antibody testing on saliva and urine specimens ,[80][81] although positive results should be confirmed with serologic testing. Rapid HIV serum testing, with results available in 3-30 minutes, has shown 99-100% sensitivity and specificity compared to ELISA when tested in clinical settings.[82]

Laboratory tests for the diagnosis of HIV infection

A person suspected to harbour HIV infection may be investigated for the with the following investigative modalities such as:[83]

1. Tests for HIV specific antibodies in serum/plasma
    - Screening tests
        - ELISA
        - Rapid test
    - Supplemental tests
        - Western blot assay
        - Immunofluorescence test
        - Line immunoassay
    - Confirmatory test
        - Virus isolation
        - Detection of HIV specific core antigen (p24)
        - Polymerase chain reaction (RT PCR/b-DNA)
2. Tests for HIV specific antibodies in the saliva
3. Tests for HIV specific antibodies in the urine

Enzyme-Linked Immunosorbent Assays/Enzyme Immunoassays

ELISA is the most commonly used type of test to screen for HIV infection because of its relatively simple methodology, inherent high sensitivity, and suitability for testing large numbers of samples, particularly in blood testing centers.[84]

A common feature of all varieties of ELISA is the use of enzyme conjugates that bind to specific HIV antibody and substrates/chromogens that produce colour in a reaction catalyzed by the bound enzyme conjugate. Various types of ELISA includes

- Indirect ELISA
- Competitive ELISA
- Sandwich ELISA

Indirect ELISA

This the most popular method of ELISA in which HIV antigen is attached to a well of a 96-well microtiter plate. Antibody in the sample is allowed to react with the antigen-coated solid support, usually for 30 minutes at 37º C or 40º C. After a wash step to remove unbound serum components, addition of a conjugate (an antihuman immunoglobulin with a bound enzyme) binds to the specific antibody that is attached to the antigens on the solid phase. Following another wash, addition of an appropriate substrate results in colour development that is detected by a spectrophotometer.[85]

Rapid tests

These tests have a total reaction time of less than 30 minutes, so they are best for emergency clinics, casualties and trauma clinics. Various technologies on which rapid tests are based includes [86]

1. Immunoconcentration (dot blot assay)
2. Immunochromatography (lateral flow assay)
3. Particle agglutination (latex, gelatin, RBCs)
4. Immunocomb (dip stick/comb test) (mostly ELISA based)

CD4 testing

The CD4 cell count in blood correlates with the risk of OIs in HIV disease, [87] and is therefore a useful marker for HIV disease staging. The CDC recommends CD4 testing every 3-6 months in all HIV-infected persons. Additionally, an inversion of the normal CD4/CD8 cell ratio, which is usually >1 in non-HIV-infected individuals is usually seen. In resource-limited settings where CD4 count may be unavailable, the total lymphocyte count (TLC), which can be determined simply and cheaply, may be used as a surrogate for CD4 in determining stage of HIV infection.[86] For example, in a cohort of HIV-positive people in south India, a TLC of <1,400 cells/μL has been shown to be a good predictor of a CD4 count <200 cells/μL and thus an appropriate surrogate marker for initiating cotrimoxazole prophylaxis. TLC may also have applications in monitoring response to antiretroviral therapy in place of or in conjunction with CD4 count. [89]

Preexposure prophylaxis

PrEP could substantially reduce HIV transmission in high-risk populations in the United States. The combination of tenofovir and emtricitabine (TDF/FTC) shows promise as pre-exposure prophylaxis (PrEP) for persons at high risk of HIV infection. Trials of TDF/FTC-based chemoprophylaxis in macaques report nearly 8-fold reductions in the risk of HIV infection.[90] In humans, recent observations in high-risk women suggest an efficacy estimate of 65%.[91] Others have noted that PrEP poses risks for

additional drug toxicity, viral resistance, and behavioural disinhibition.[90] However, the long-term impact of PrEP on transmission, behaviour, clinical in outcomes, and cost has not been studied. Given recent disappointments HIV prevention and vaccine development, further study of PrEP-based HIV prevention is warranted. [91]

Now trials were conducted in using preexposure prophylaxis in serodiscordant couples to prevent HIV transmission. [92]

Aim of the Study and Materials& Methods

Aim

Aim of the study / objectives of the study

- To study the prevalence of both HIV seropositive concordance and discordance among couples attending Institute of Venereology using rapid method.
- To study epidemiological characters of HIV infected couples
- To identify the factors that are likely to influence HIV transmission among married couples.
- To study the pattern of sexually transmitted infections among both concordant and discordant HIV infected couples.

Materials & Methods

Study design

Cross sectional study.

Sample:

100 HIV patients and their married partners attending Institute of Venereology from November 2010 to November 2011 are randomly recruited for the study.

Inclusion Criteria:

- HIV seropositive individual and their married partner attending Institute of Venereology.

Exclusion criteria:

- HIV infected individual who is not willing to disclose their personal history or not willing to bring their partner.
- High risk group such as commercial sex workers, transgenders.

Methods:

HIV seropositive index case and their partner are interviewed at outpatient department in privacy and in confidential manner. A structural questionnaire is administered to the patient after getting signed consent. The questionnaire includes questions related to demographic characters, sexual behaviours and history of previous sexually transmitted infections. In sexual history the patients were asked about homosexual, bisexual behaviour, sexual practice, premarital, extramarital contact and condom usage. The history of presenting complaints, past STIs' and their treatment are recorded.

The clinical staging of HIV seropositive index cases done after medical examination, based on World Health Organization (WHO) clinical staging of HIV. Physical and genital examination done to find out any genital or extra genital evidence of STI's.

The STIs' in these patients are diagnosed with clinical findings and relevant lab investigations.

In case of genital ulcers

Dark field examination for Treponema pallidum

Tzanck test for giant multi nucleated epithelial cells.

Gram stain for Haemophilus ducreyi and Candida

Tissue smear and Leishman's stain for klebsiella granulomatis

10% KOH examination

In case of urethral discharge or burning micturition

Gram stain examination of urethral smear for gonococci.

Urethral swab or urine for gonococcal culture.

Urine culture using Cled media.

Vaginal discharge of all female patients examined for :

Wet mount microscopy for Trichomonas vaginalis.

10% KOH preparation for Candida albicans.

Gram stain of vaginal smear for clue cells and Candidal hyphae.

Gram stain of endocervical smear for gonococci.

In addition to above investigation endocervial swab for gonococcal culture are collected for all female patients.

Blood samples were collected for performance of the serological tests, which includes

HIV Rapid Method (strategies 3)

VDRL if positive confirmed by TPHA

The result of HIV are given only after post test counselling.

Observations

Results

Data collected is analysed using Chi-square, the statistical significance was considered if P value < 0.05.

Serostatus of the couples with respect to HIV

A total of 100 HIV seropositive individuals and their married partners were examined in this study. Among the 100 married couples 65 couples were seroconcordant for HIV (both husband and wife were positive) whereas 35 couples were serodiscordant for HIV(either husband or wife is positive).

Table. 5. Serostatus of the couples

Serostatus	**No. Of couples**	**Percentage**
Seroconcordance	65	65%
Serodiscordance	35	35%
Total	100	100%

- Among that 35 HIV serodiscordant couples, males alone positive in 29 couples and females alone positive in 6 couples.
- Among 100 males 94 were positive for HIV.
- Among 100 females 71 females were positive for HIV.

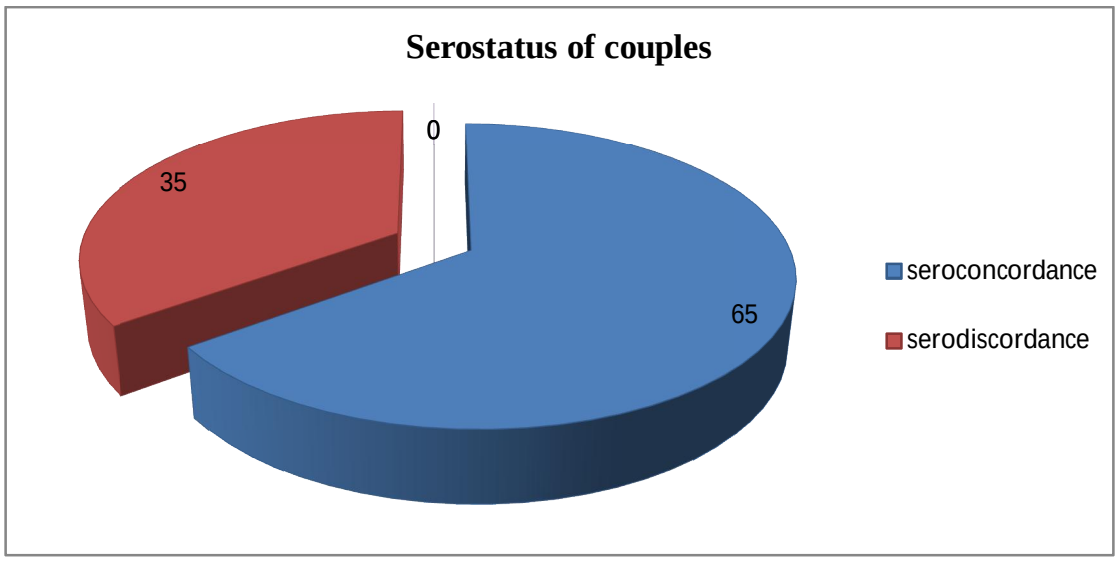


Fig. 1. Serostatus of the couples

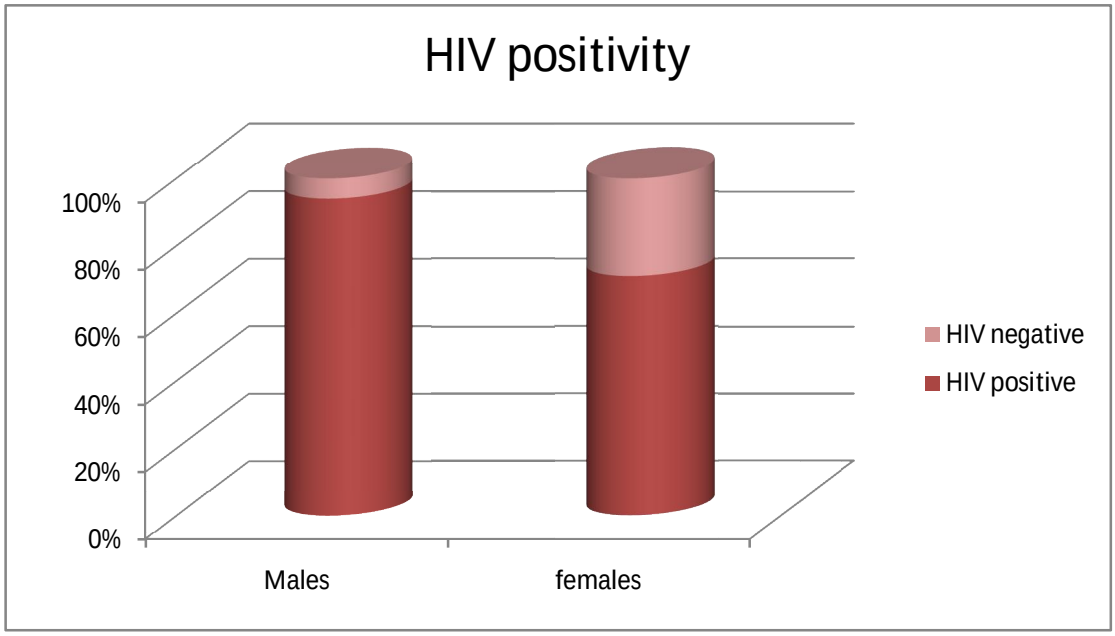


Fig 2 HIV reactivity in males and females

1) Evaluation of epidemiological factors of HIV infected couples:

a) Age distribution among study couples

A total of 100 married couples which includes 100 males and 100 females were recruited for this study. The age distributions among them were as follows:

Table1.Age distribution among the couples

Age group	Total number of males	Total number of females	percentage
18-25	1	14	7.5
26-35	29	37	33
36-45	45	39	42
46-55	19	10	14.5
56-65	6	0	3
Total	100	100	100

b) Area of residence

Most of the couples were from urban areas which constituted 68% and the rural inhabitants constituted about 32%.

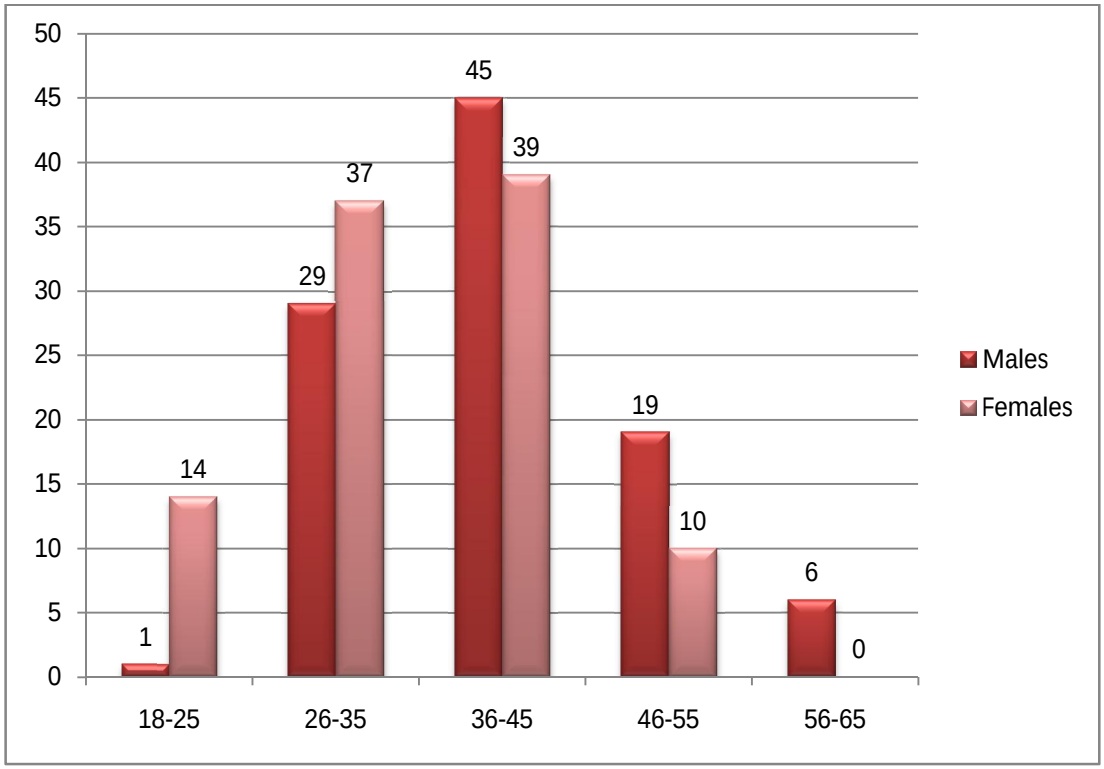


Fig.3. **Age distribution among study couples**

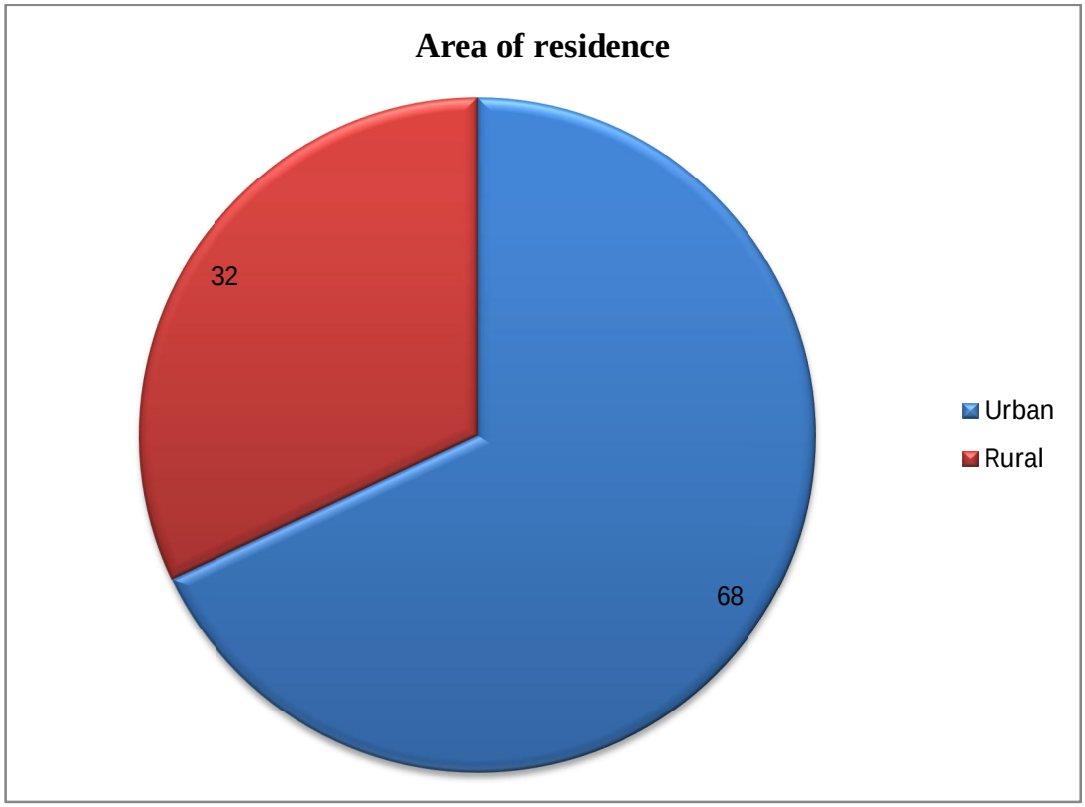


Fig. 4. Area of reside

c) Educational status

In the study population majority of the males had an educational status which lie between 6^{th} to 12^{th} standard whereas majority of the females were illiterate.

Table. 2. Educational status

Educational status	Number of males	Number of females	Total percentage
illiterate	16	41	28.5%
<5^{th} std	24	18	21%
5^{th} -12^{th} std	56	38	47%
Graduate	4	3	3.5%
Total	100	100	100%

d)Monthly income

In this study, majority of the couples (67%) had a monthly income in the range of Rs. 2000 to 5000. About 33% of the couples had a low income of about 2000 or below. None of our patients had a monthly income greater than Rs.5000.

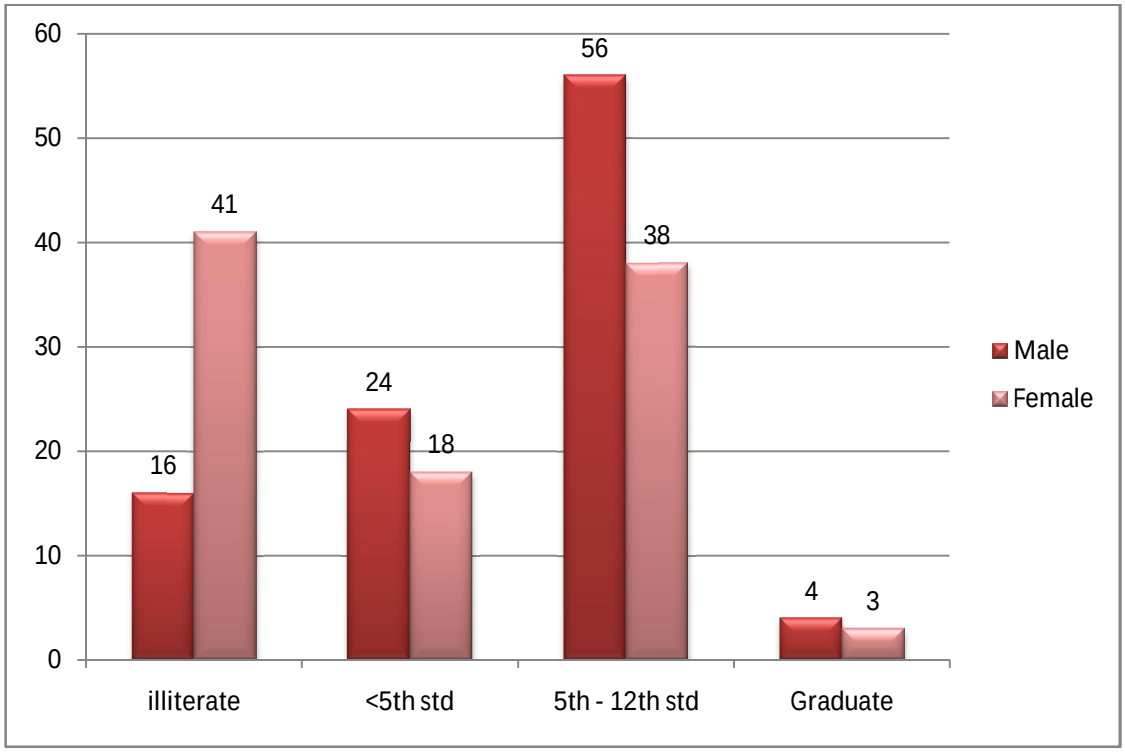


Fig. 5. Educational status

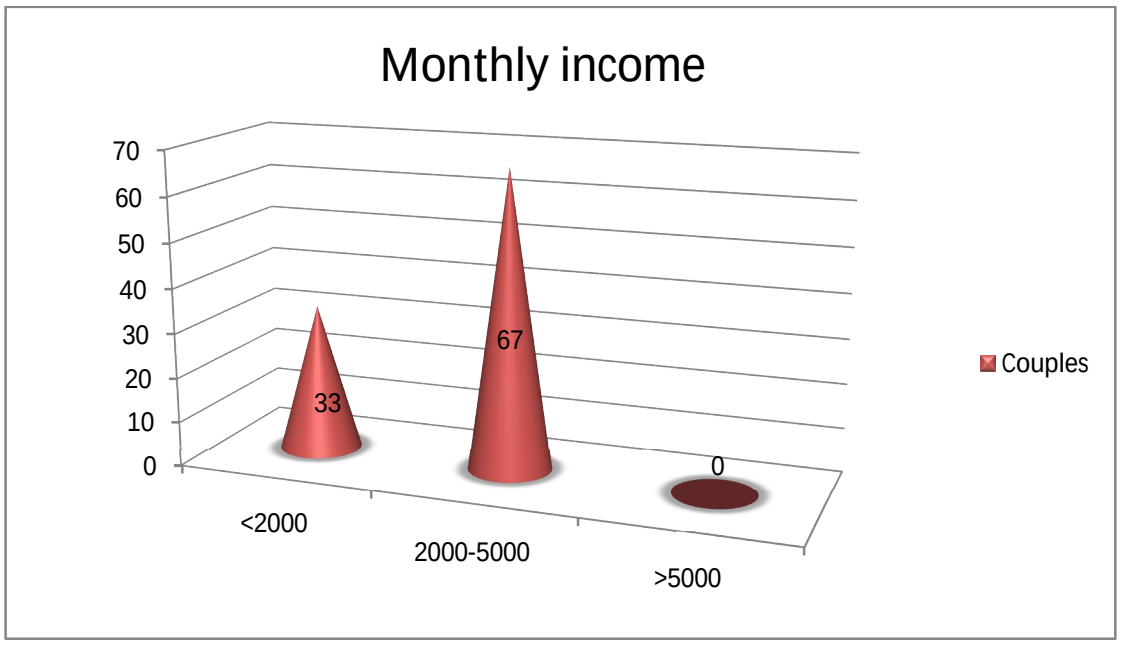


Fig. 6. Monthly income

e) **High risk behaviours**

Majority males and few females of our study population had history of high risk sexual behaviours. We studied them under the broad divisions under the heading contacts with commercial sex workers, homosexuals, and any known person. The data is tabulated is as follows:

Table. 3. High risk behaviours

High risk behaviours	**High risk sexual behaviour (sexual contact other than married partner)**		**percentage**	
	Males	**Females**	**male**	**female**
Commercial sex workers (CSW)	84	0	84%	0
Homosexuals	9	0	9%	0
Known person	7	6	7%	6%
Denies history	8	94	8%	94%
Total	100	100		

A larger proportion of the males (84%) had high risk sexual behaviours both before and after marriage with the commercial sex workers. 9% of them had history of contact with homosexuals. Only 6% of the females had history of sexual contact with person other than their married partner .

f) Possible routes of HIV acquisition in index cases

In this study 90% of the couples had a heterosexual orientation while 8% were bisexual. Two of the couples denied high risk behaviour and had history of blood transfusion.

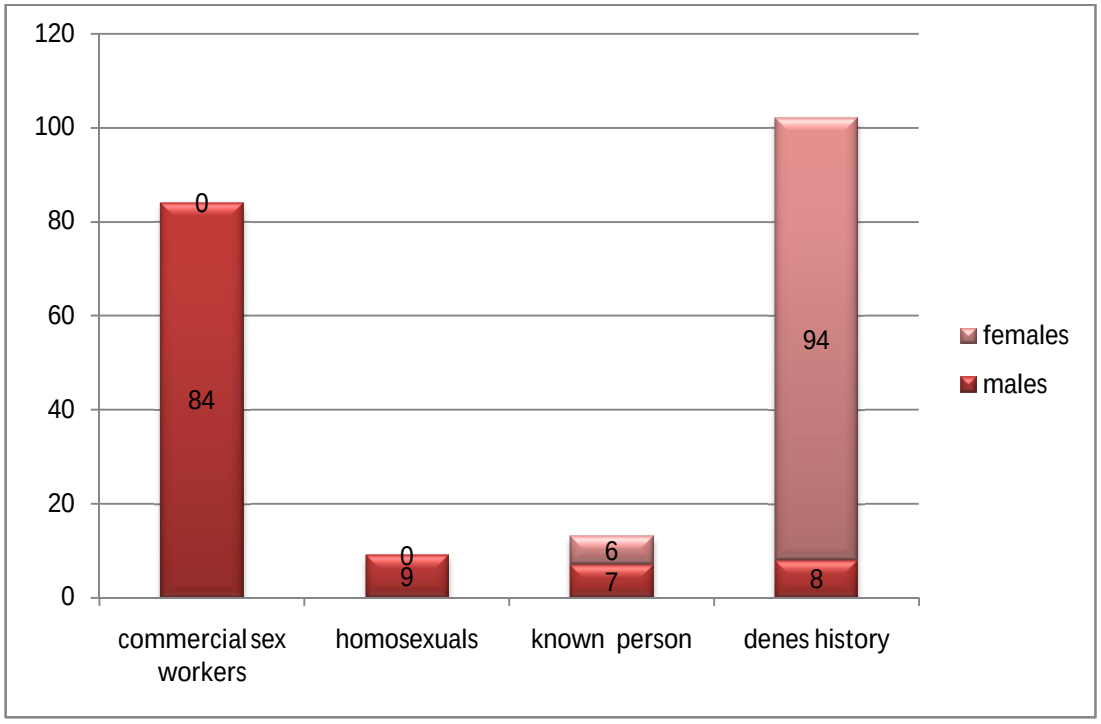


Fig. 7. High risk behaviours

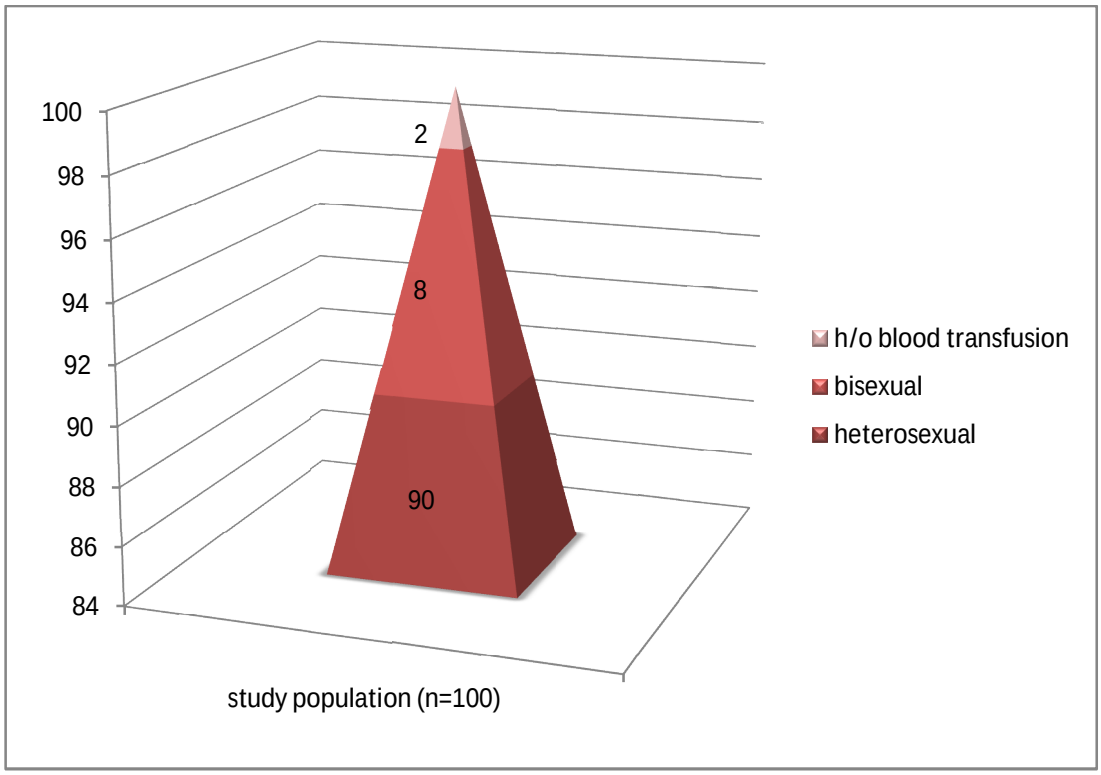


Fig.8. Routes of HIV acquisition

g) Reason for HIV testing in index cases

Among the index cases 92 were males and 8 were females. The reasons for HIV screening was studied under the following headings and the observations were as follows:

Table. 4. Reason for HIV testing in index cases

Reason for HIV testing in index cases	Males	Females
High risk behaviour	10	Nil
Presence of STI	18	2
Antenatal screening	Nil	2
Referred from other departments	64	4
Total	92	8

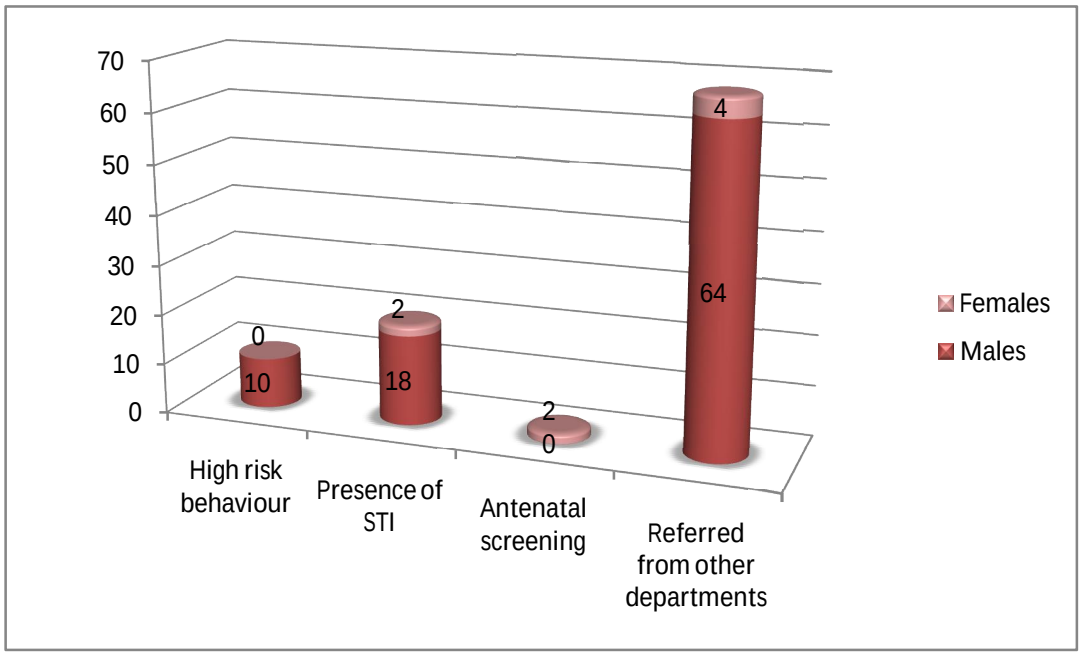


Fig. 9. Reason for HIV testing in index cases

2) EVALUATION OF THE VARIOUS RISK FACTORS IN RELATION TO THE HIV SEROCONCORDANCE AND SERODISCORDANCE OF THE COUPLES

a) Duration of marital contact

The number of years that a couple was together after they got married was studied under the following range groups namely <5 years, 5 to 10 years, 11 to 15 years and >15 years. The proportion of couples who were seroconcordant increased with the increase in their years together they spent after marriage but the proportion was statistically insignificant.

Table. 6. Duration of marital contact

Married since	Frequency	Outcome		Total
		Discordance	Concordance	
<5 years	19	9(47.4%)	10(52.6%)	19
5 to 10 years	31	11(35.5%)	20(64.5%)	31
11 to 15 years	22	8(36.4%)	14(63.6%)	22
>15 years	28	7(25.0%)	21(75.0%)	28
Total	100	35	65	100

The statistical analysis by Pearson's Chi squared test is p value is 0.470 (>0.05).

b) Number of sexual contacts per week

- 12 of the study couples had around <=1 sexual contact per week with their partner. Of these couples 3 were seroconcordant and 9 were serodiscordant.
- 75 of the couples had 2 to 3 sexual contacts per week. Among that 51 couples were seroconcordant and the remaining 24 were serodiscordant.
- 13 couples had >=4 times sexual contact per week with their sexual partners. Among that 11 couples were seroconcordant and the remaining 2 were serodiscordant.

Table.7. Number of sexual contacts per week

Sexual contacts per week	Frequency	Outcome		Total
		Discordance	Concordance	
<=1	12	9(75.0%)	3(25.0%)	12
2 to 3	75	24(32.0%)	51(68.0%)	75
>=4	13	2(15.4%)	11(84.6%)	13
Total	100	35	65	100

The data was statistically insignificant after analysis by Pearson's Chi-Square p value is 0.404 (>0.05)

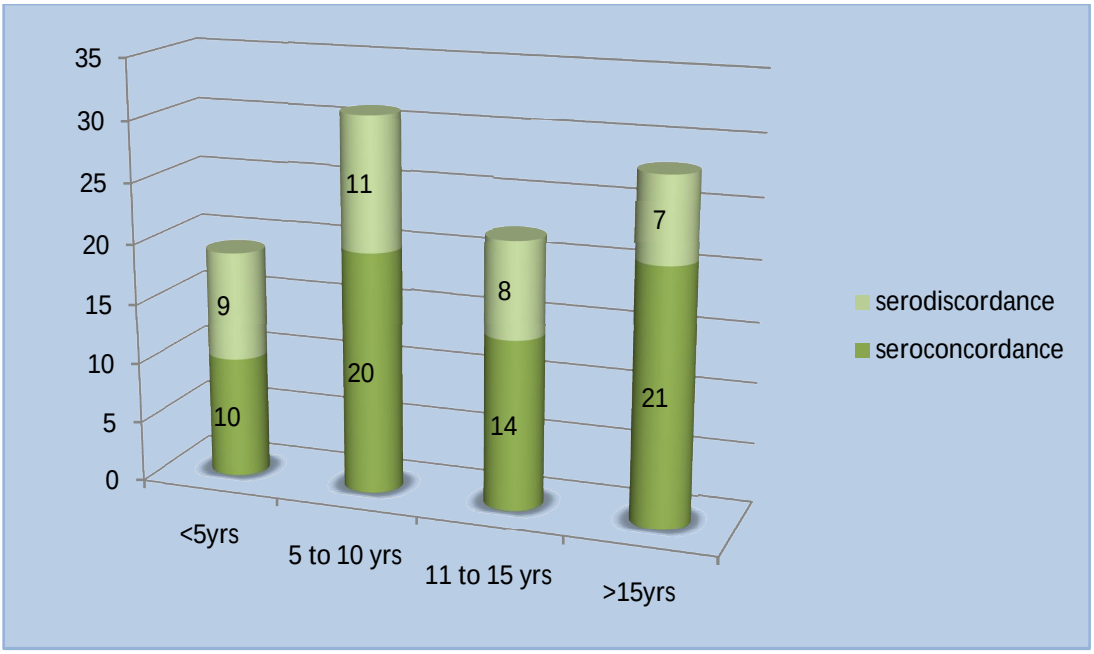


Fig. 10 Duration of marital contact

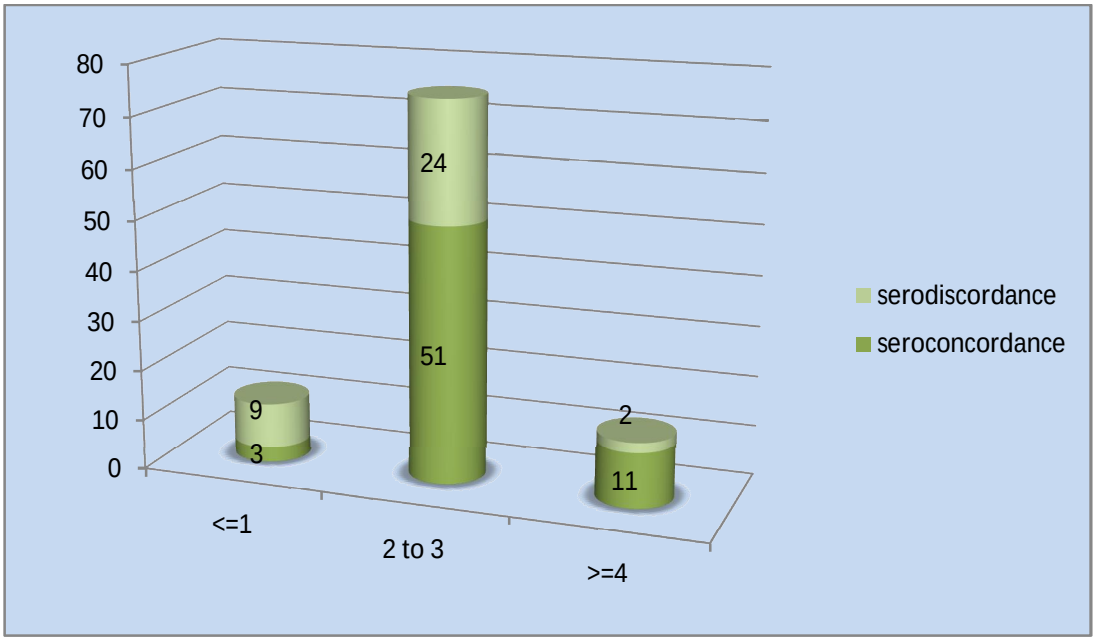


Fig. 11. Number of sexual contacts per week

C) HIV staging

The HIV staging was done according to the WHO classification. For statistical analysis the stages 1 and 2 were considered together as early and stage 3 and 4 as late. They were then together compared with the serostatus data.

Table.8. HIV staging

HIV Stage grouping	Frequency	Outcome		Total
		Serodiscordance	Seroconcordance	
Early (1+2)	71	32(54.9%)	39(45.1%)	71
Late (3+4)	29	3(10.3%)	26(89.7%)	29
Total	100	35	65	100

The statistical analysis by continuity correction was significant p value is <0.05

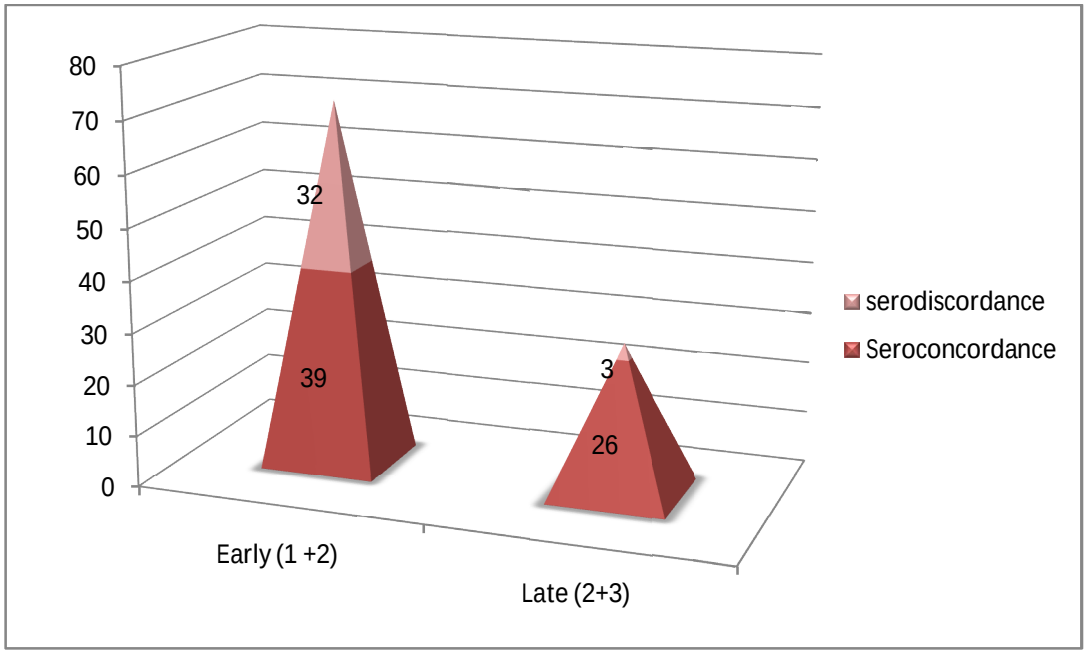


Fig. 12. HIV stage grouping

d) Patients under ART

Among all the 100 couples only 12 were under ART, while two of the couples were defaulters. Of the 12 couples who were under the treatment 6 were seroconcordant and 6 were serodiscordant.

Table. 9. Patients under ART

ART	Frequency	Outcome		Total
		Discordance	Concordance	
No	88	29(33.7%)	57(66.3%)	88
Yes	12	6(50%)	6(50%)	12
Total	100	35	65	100

The statistical analysis by continuity correction is p value is 0.517 (>0.05)

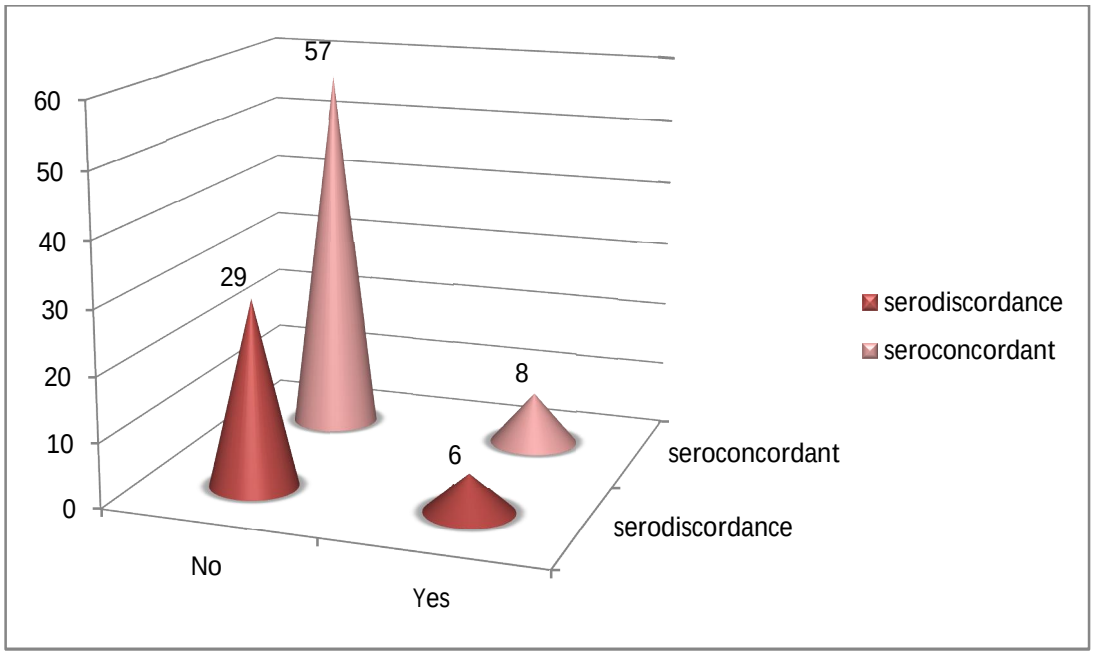


Fig. 13. Patients under ART

e) Condom usage

Most of the study population (74%) have never used condom during their sexual acts. 23% of the couples used condom occasionally whereas 3% were unaware about the usefulness of condom.

Table. 10. Condom usage

Condom usage	Frequency	Outcome		Total
		Discordance	Concordance	
No	77	17(22.1%)	60(77.9%)	77
Yes	23	18(78.3%)	5(21.7%)	23
Total	100	35	65	100

The statistical analysis by continuity correction is p value is <0.05

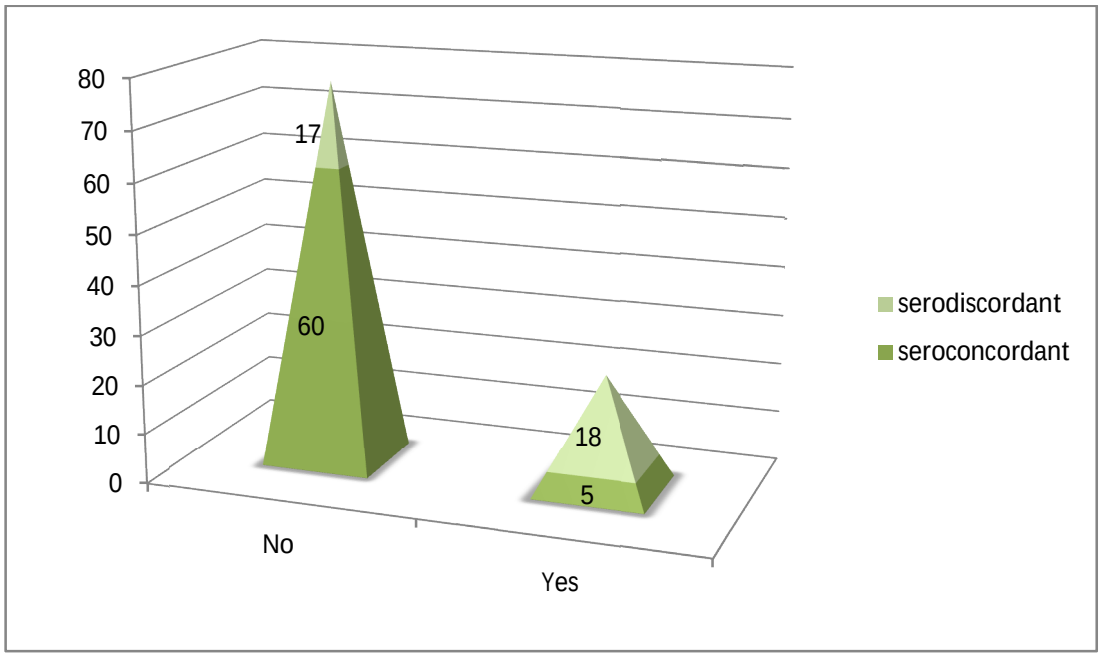


Fig. 14. Condom usage

f) Role of circumcision

In this study 7 males had underwent circumcision whereas the rest of the population [93] had not been circumcised. Of the 7 males with circumcision 1 was seroconcordant and 6 were serodiscordant.

Table. 11. Role of circumcision

Circumcision	Frequency	Outcome		Total
		Discordance	Concordance	
No	93	29(31.2%)	64(68.8%)	93
Yes	7	6(85.7%)	1(14.3%)	7
Total	100	35	65	100

The statistical analysis by continuity correction is p <0.05 (0.012)

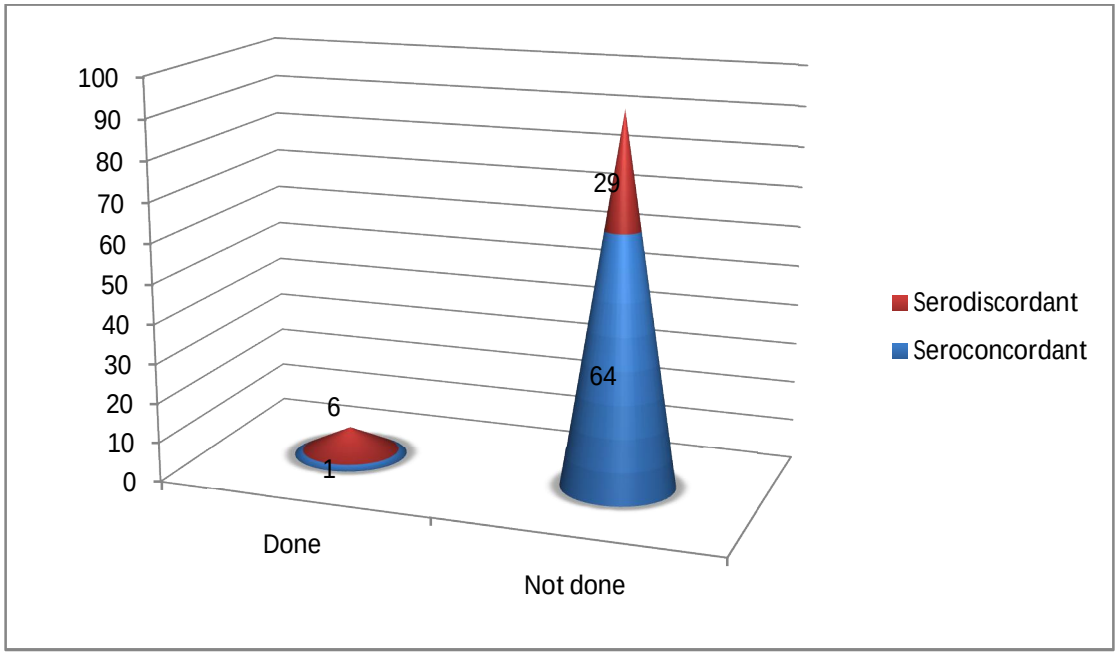


Fig. 15. Role of circumcision

g) Practise of oral sex

All the patients in the study denied having oral sex with their partners.

h) Practice of anal sex

Anal sex was practiced by about 35 of the study population whereas 65 of the couples denied the anal sexual practise. Out of those who practiced anal sex 5 were serodiscordant and the remaining 30 were seroconcordant.

Table.12. Practise of anal sex

Anal sex	Frequency	Outcome		Total
		Discordance	Concordance	
No	60	34(56.7%)	26(43.3%)	60
Yes	40	1(2.5%)	39(97.5%)	40
Total	100	35	65	100

The statistical analysis by continuity correction is p value is <0.05 (0.00).

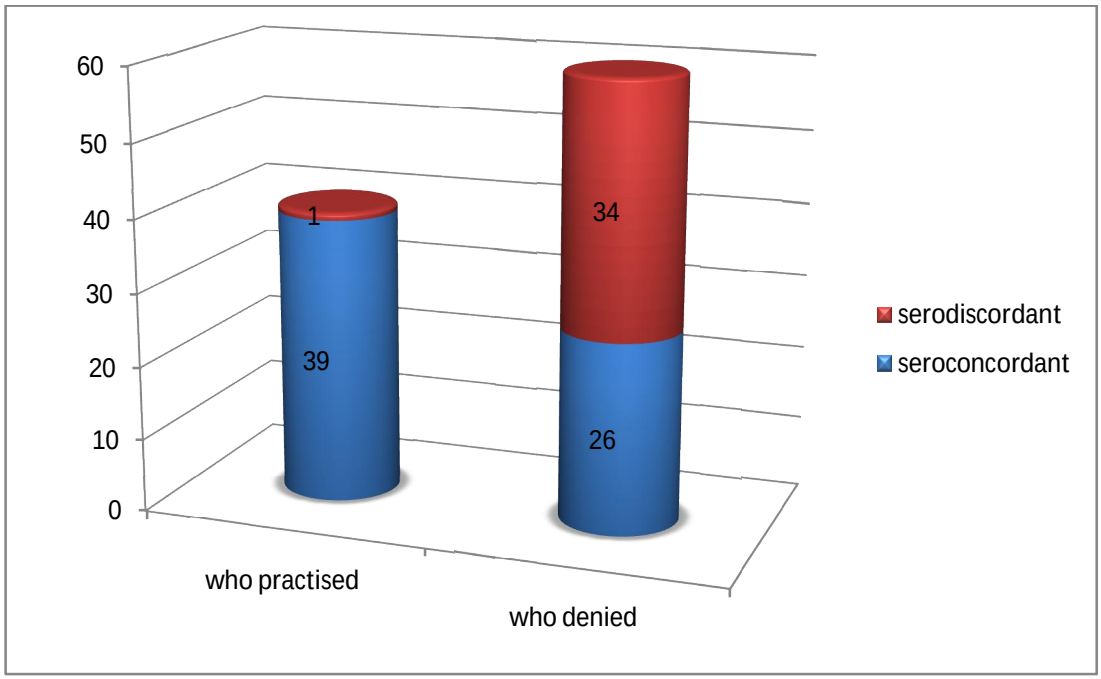


Fig . 16. Practise of anal sex

i) Sex during menstruation

Thirty eight couples had a history of having sex during the menstrual phase of their female partner among which 37 of them were seroconcordant and 1 was serodiscordant.

Table. 13. Sex during menstruation

Sex during menstruation	Frequency	Outcome		Total
		Discordance	Concordance	
Yes	38	1(2.6%)	37(97.4%)	38
No	62	34(54.8%)	28(45.2%)	62
Total	100	35	65	100

The statistical analysis by continuity correction (2x2) table is p value is <0.05

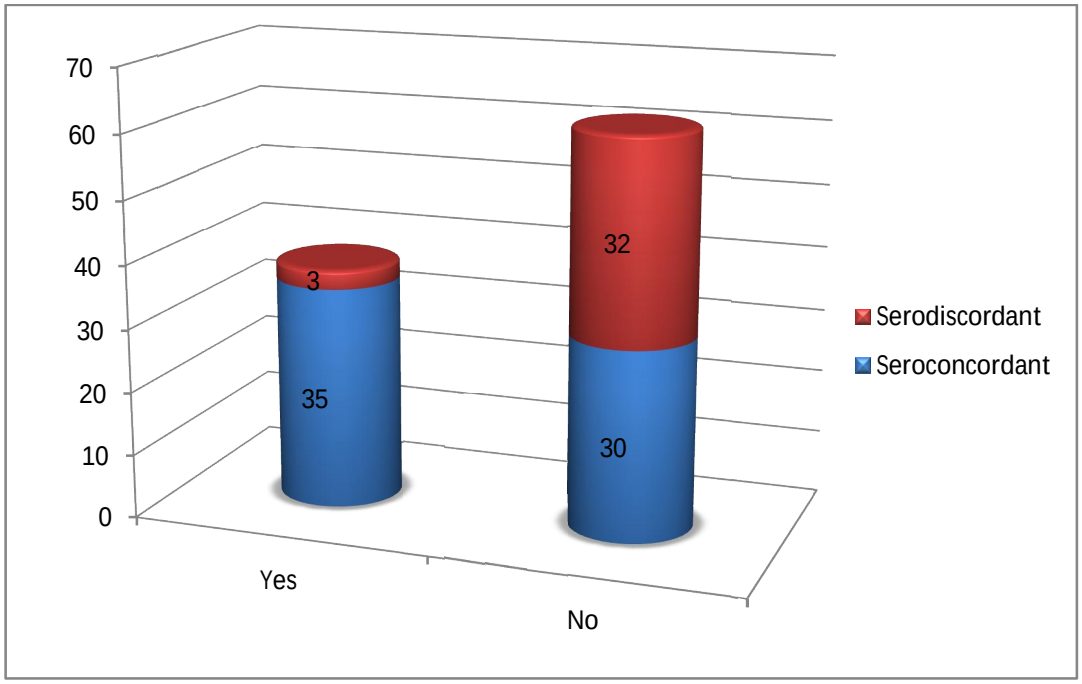


Fig. 17. Sex during menstruation

3) Analysis of the presence of sexually transmitted diseases and its relation to the HIV serostatus of the couples:

1)Previous venereal diseases (PVDs)

History of previous STIs were found in the following number of patients:

Table. 14. Previous veneral diseases (PVDs)

PVDs	HIV seroconcordance	HIV serodiscordance	Males	Females	Total
Genital ulceration	17	2	16	3	19
Urethritis	5	1	6	0	6
Balanoposthitis	3	2	5	0	5
Vaginal discharge	3	1	0	4	8
Total	31	6	27	7	38

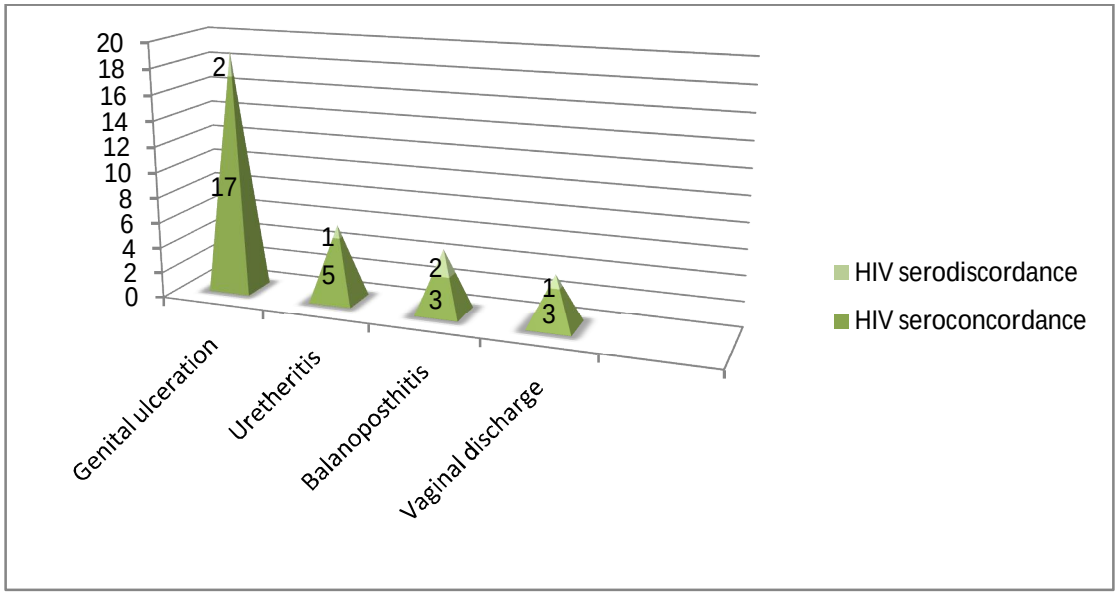


Fig.18. Distribution of PVDs in the study population

PVD in males

Among the study population 27 males had a positive history of having one of the listed veneral diseases whereas the remaining 73 males had a negative history.

Table. 15. PVD in males

PVD males	Outcome		Total
	Discordance	Concordance	
No	31(42.5%)	42(57.5%)	73
Yes	4(14.8%)	23(85.2%)	27
Total	35	65	100

The statistical analysis by continuity correction is significant p value is <0.05

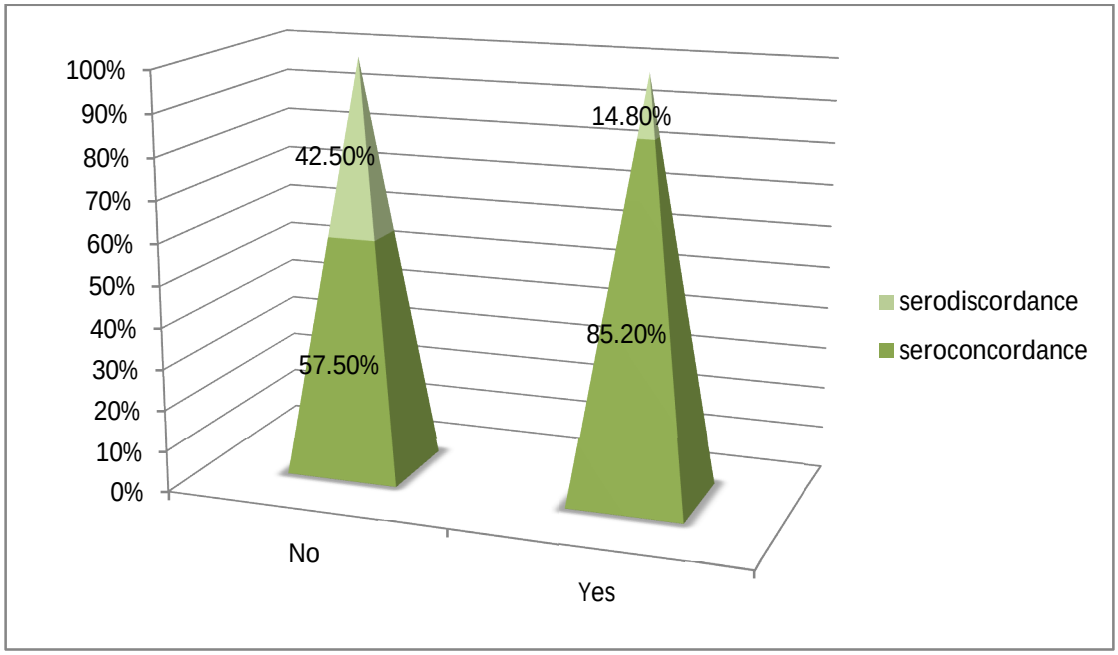


Fig. 19. PVD in males

PVD in females

Among the study population 7 females had a positive history. The remaining 93 females did not have any history of previous venereal diseases.

Table. 16

PVD wife	Outcome		Total
	Serodiscordance	Seroconcordance	
No	34(36.6%)	59(63.4%)	93
Yes	1(14.3%)	6(85.7%)	7
Total	35	65	100

PVD in females

The statistical analysis by continuity correction was not significant p value is >0.05

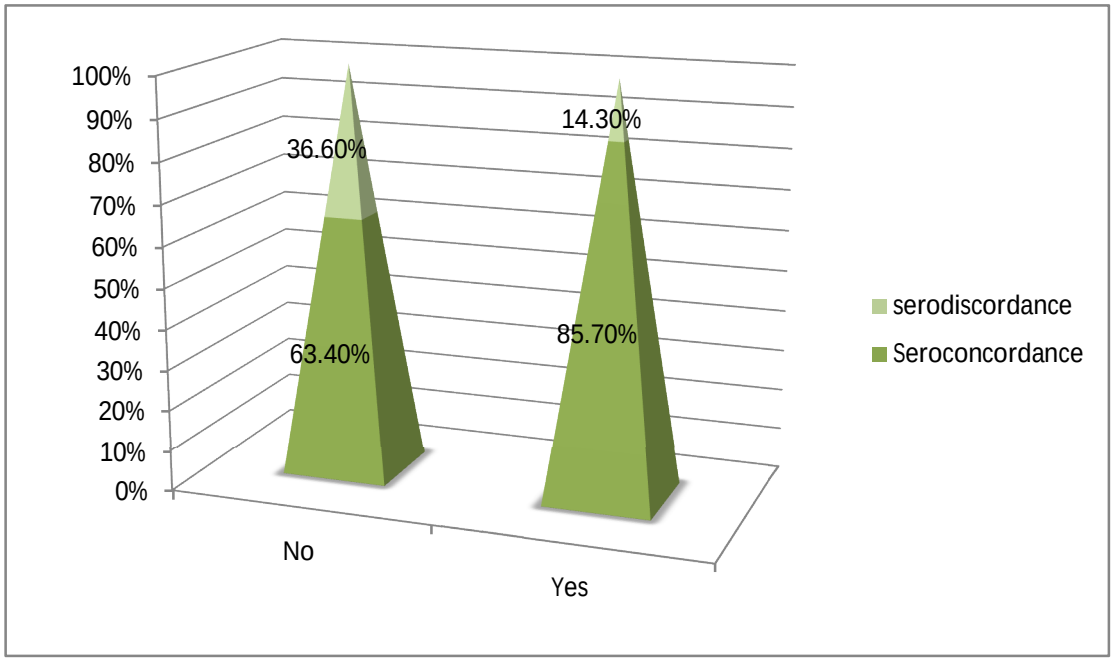


Fig. 20. PVD in females

2) Sexually transmitted infections:

The occurrence of various sexually transmitted diseases diagnosed by clinical and necessary lab investigations and was distributed as follows:

The most common STI in the males was genital ulcer disease whereas in the females it was bacterial vaginosis.

Table.19. STIs distribution

STIs	HIV seroconcordance	HIV serodiscordance	Males	Females	Total
VDRL reactivity	12	4	9	7	16
Herpes genitalis	7	0	5	2	7
Ano-genital wart	9	3	11	1	12
Non-specific genital ulceration	11	1	8	4	11
Non-specific urethritis	7	2	9	0	8
Candidal balanoposthitis	5	2	7	0	6
Vulvovaginal candidiasis	7	2	0	9	9
Bacterial vaginosis	11	3	0	14	14
Trichomonas vaginalis	6	1	0	7	7
Cervicitis	8	1	0	9	9
Bartholin's abscess	0	1	0	1	1
Total	82	21	49	54	100

Sexually transmitted infections in males:

Among the 40 males who had STIs, 9 males had mixed venereal diseases. Among that 8 males (88%) belong to HIV seropositive concordant while 1(12%) males were HIV seropositive discordant.

Table. 17. STI in males

STI in husbands	Outcome		Total
	Seroconcordance	Serodiscordance	
Yes	33(82.5%)	7(17.5%)	40
No	35(58.3%)	25 (41.7%)	60
Total	68	32	100

Statistical analysis by continuity correction is significant p value is <0.05

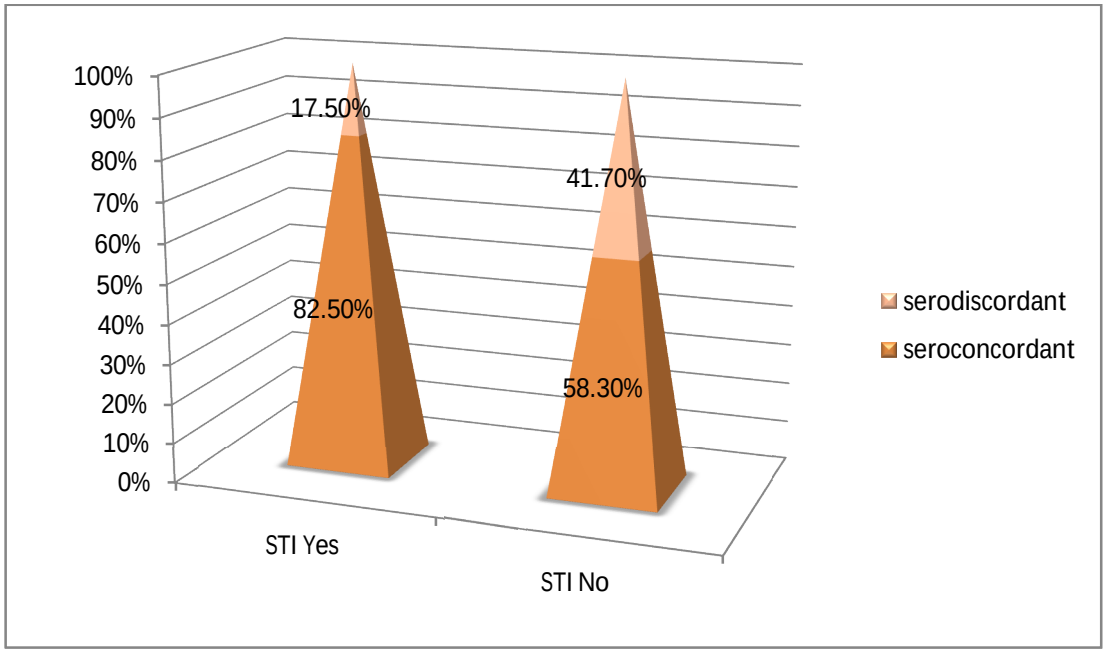


Fig. 21. STI in males

e) STI in females

Sexually transmitted infection was present in 39 females whereas it was absent in the remaining 61 females. Among the 39 females who had STIs 10 females had multiple venereal diseases. 9 among them belong to HIV positive seroconcordant group while 1 belong to HIV seropositive discordant group.

Table. 18. STI in females

STI females	Outcome		Total
	Seroconcordance	Serodiscordance	
No	30(49.2%)	31(50.8%)	61
Yes	35(89.7%)	4(10.3%)	39
Total	65	35	100

The STIs in females were statistically significant by continuity correction p value is <0.05

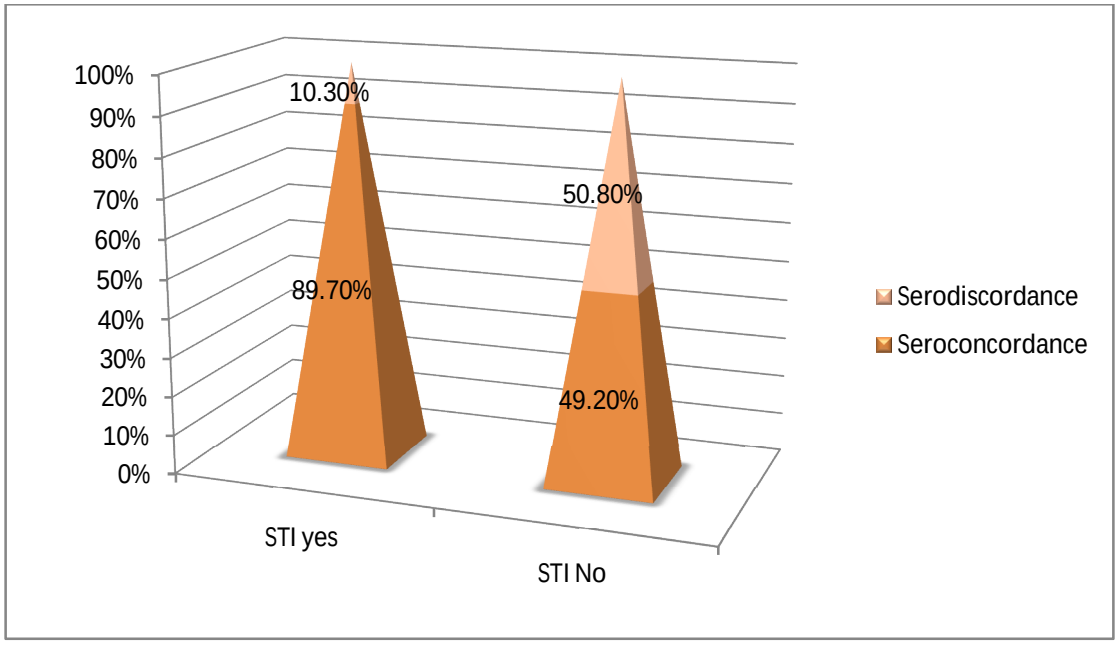


Fig. 22. STI in females

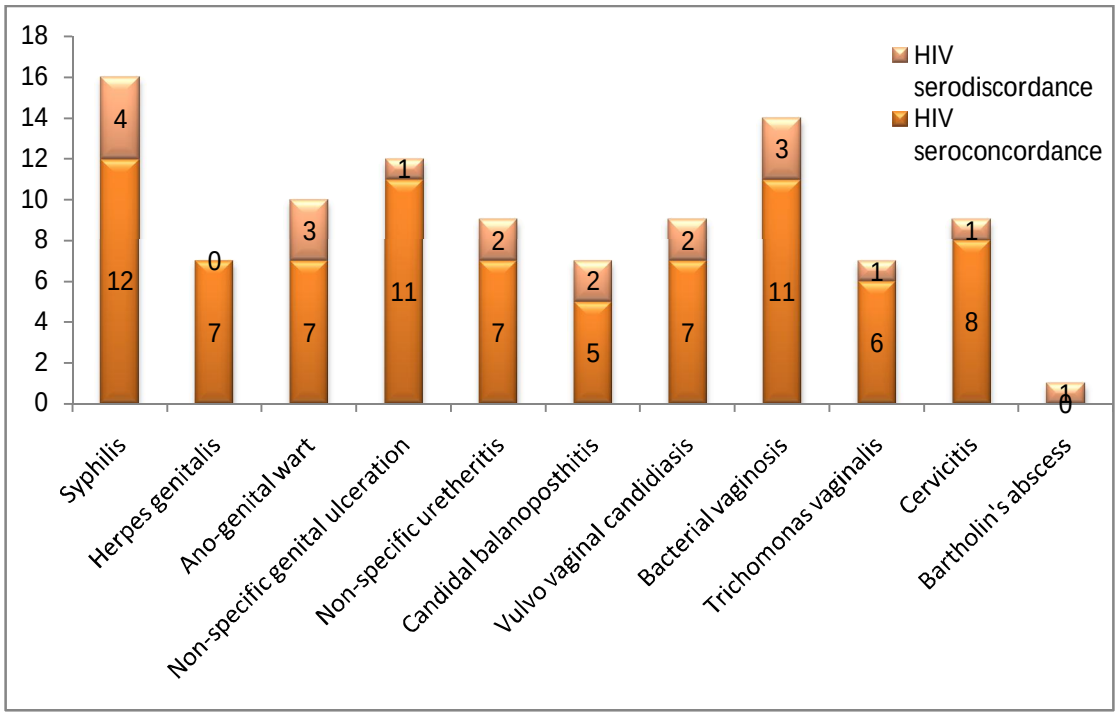


Fig.23. STIs distribution

Genital wart in HIV positive male

Genital wart in HIV positive male

Genital wart with erosion

Perianal wart in HIV positive male with homosexual activity

Perianal ulceration in HIV positive male with homosexual activity

Candidal balanoposthitis in HIV positive male

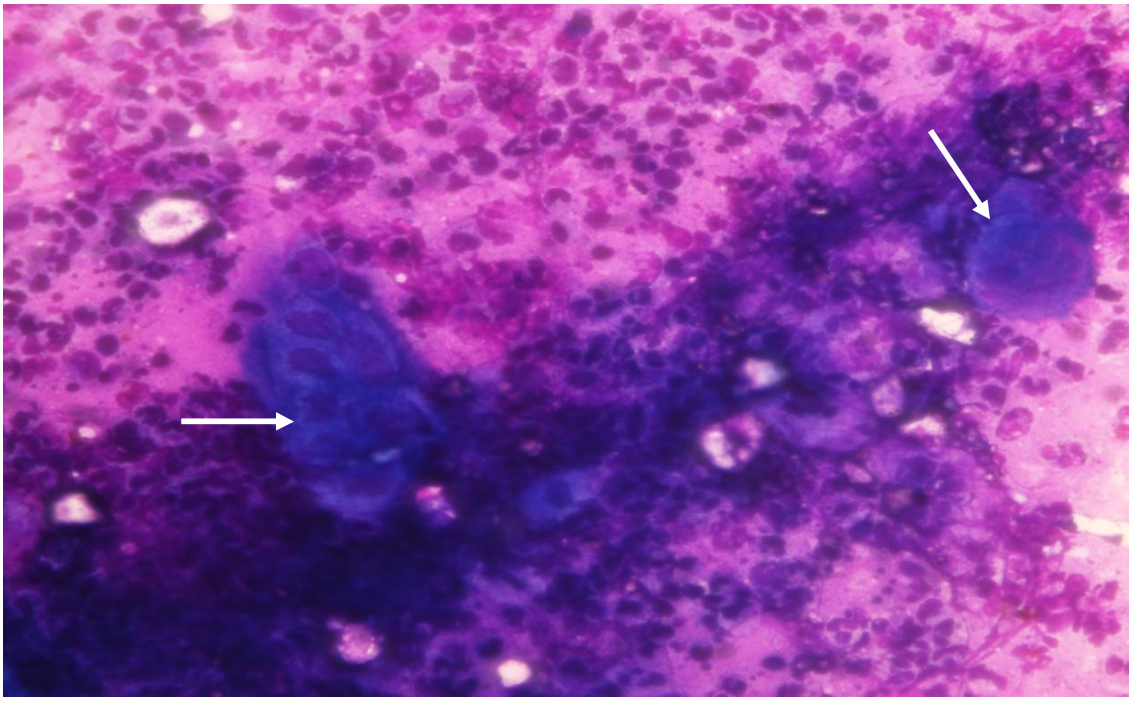
HIV positive male(concordant male) with healed genital scar (VDRL reactive in 1 in 32 dilution)

HIV positive male(concordant couple) with genital herpes

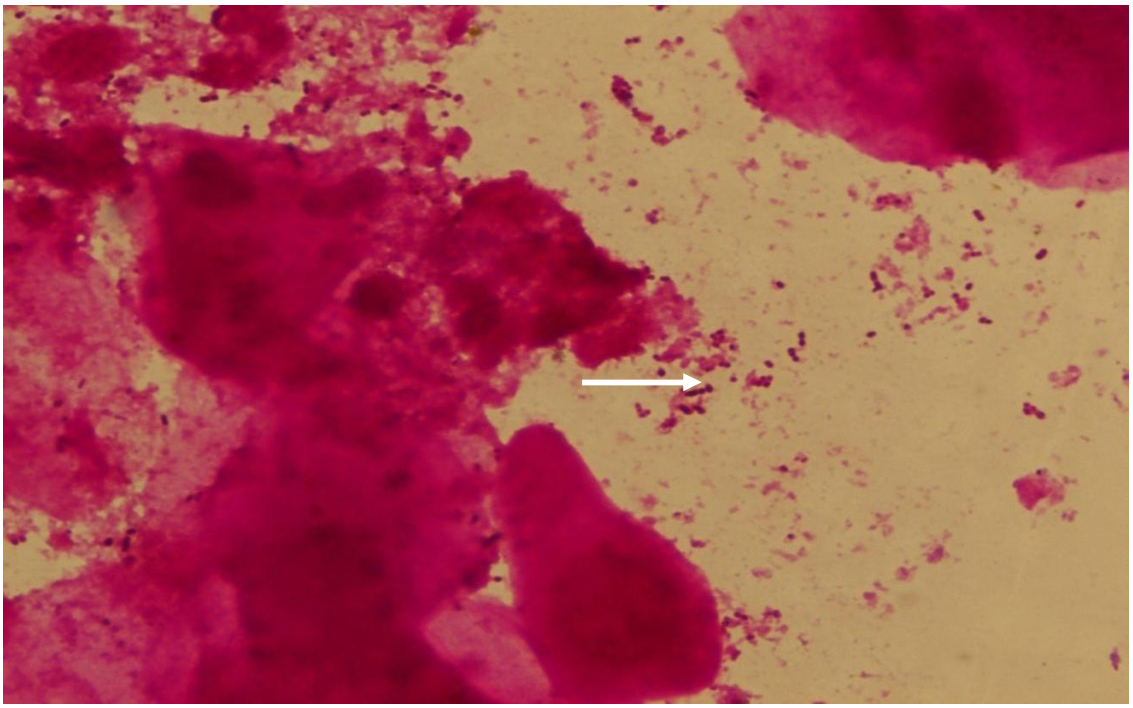
HIV positive female genital ulceration

HIV positive female (concordant couple) with ulceroproliferative growth over external genitalia

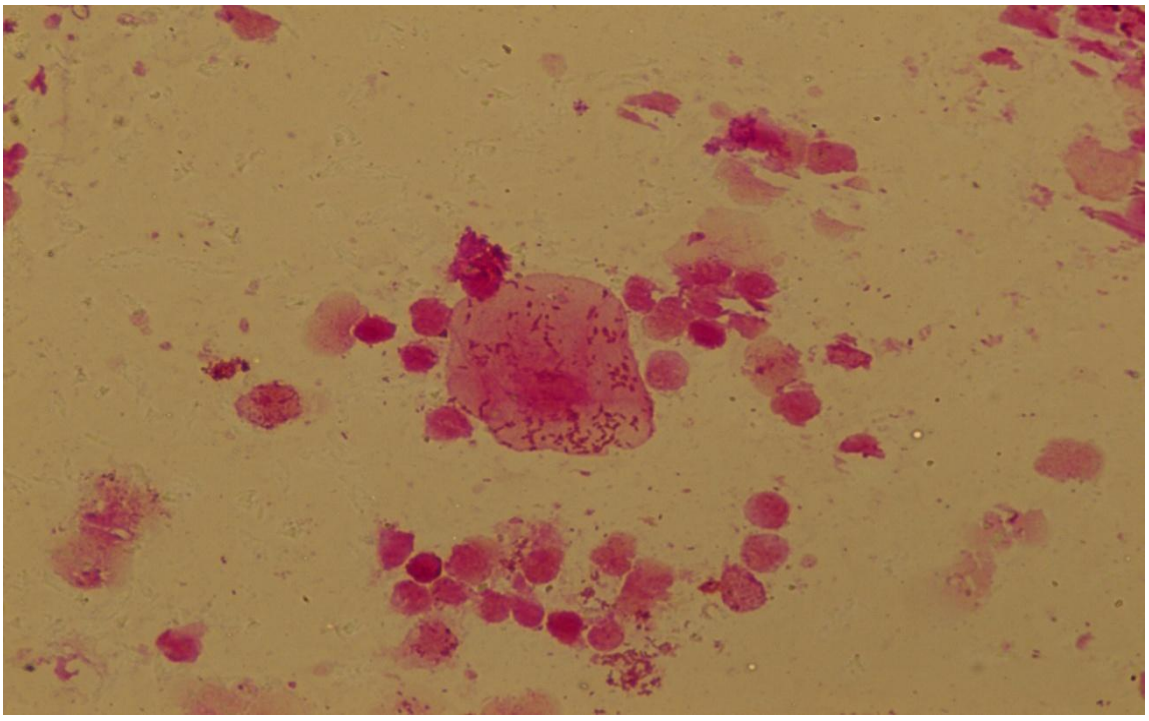
HIV positive female (concordant couple) with perianal herpes



Tzanck smear showing multinucleated giant cell



Grams stain showing candidal spores



Grams stain showing clue cell

Discussion

Discussion

A hundred HIV patients and their married partners attending Institute of Venereology, Madras Medical College were randomly recruited for this study. All the patients were interviewed in privacy using a structured questionnaire after getting their signed consent, and the data thus obtained was tabulated and their statistical analysis is as follows:

Serostatus of the couples

In this study 65% of the couples were HIV positive seroconcordance and 35% of the couples were HIV serodiscordant. Which was similar to study conducted in Baroda[100] (72.4% were seroconcordance while 27.6% were serodiscordant). This shows the increase in transmission of HIV infection through intimate sexual relationships. Majority of the index cases are males, therefore females are vulnerable to new infections. So, prevention measures should be targeted towards these population groups. [101]

Age distribution

The mean age of males and females in this study was 40.5 and 34 years respectively. The total mean age was 37 years. The findings are similar to those observed in the studies conducted in Kashmir.[93] Similar studies conducted in Eastern India[94] had a mean age of 32.6 which is lower than this study. This observation can be attributed to this study population being only married couples and the exclusion of the paediatric and the adolescent population. In this study 75% belonged to the age group of 25 to 45 years and

similar observations was found in the clinico-epidemiological study conducted on HIV patients in Trivandrum. [95]

Area of residence

Most of the couples were from urban areas which constituted 68% and the rural inhabitants constituted about 32%. This can be attributed to the low awareness about HIV disease among the rural population. [96]

Educational status

In this study population majority of the males had an educational status which lie between 6^{th} to 12^{th} standard whereas majority of the females illiterate. About 47% of all the study population had a secondary level of education and 28.5% were illiterate. Only 3.5% of the population were graduates. In a study conducted in rural areas of the Saurashtra region of Gujarat, India it was found that the basic knowledge of HIV/AIDS is still lacking in about two fifths of the rural population. Literacy and media exposure are definitive factors that determine awareness of HIV among them.[96]

Monthly income

In this study majority of the couples had a monthly income in the range of Rs. 2000 to 5000. None of our patients had a monthly income greater than Rs.5000. People with low literacy and poor family have higher risk of HIV. Majority of these populations are in their productive age group and therefore it affects the economic status of the family and also the country. [43]

High risk behaviours

In this study 84% of the males give history of exposure to CSWs. Several studies conducted in India show a similar finding. [97][98] Only 6% of the female population had a positive history of high risk behaviour which suggests that majority of the females acquire the infection mainly from their husbands or intimate partners.[1] There were 7% of males with homosexual activities and thereby serve as the bridge population in transmitting the disease to their female partners.[5]

Modes of acquisition of HIV in the index cases

About 92% of the index cases acquired HIV through heterosexual contacts whereas 8% were bisexuals and the remaining 2% had history of blood transfusion. These findings correlate with many studies in the South Indian region which confirm that heterosexuality to be the primary mode of transmission.[99]

Reason for HIV testing in index cases

In relation to this study findings of more than 90% of the index cases having history of high risk behaviour only 10% of them came for HIV screening on the first hand. The same scenario was observed in those with STIs (observed 40% in males and 39% in the females). This suggests the lack of awareness and initiative among the population at risk towards HIV.[96]

Married since and number of sexual contacts per week

Though statistically insignificant, the proportion of concordance significantly increased across the category of number of years of marital relationship and frequency of sexual contact per week. A cross sectional studies conducted in Europe have corroborated similar finding.[102]

HIV staging

Advanced HIV disease (stage 3 and stage 4) were significantly associated with seroconcordance of the couples. Similar findings have been seen in various other cross sectional studies conducted in Zimbabwe and Zambia.[103][104] Anderson has also demonstrated that higher quantities of viral particles are found in genital secretions of patients with advanced HIV disease compared to asymptomatic patients.[106]

ART therapy

Various studies depicted initiation of ART therapy can prevent HIV transmission from index case to partner. [103][106] In this study role of ART in HIV transmission were not statistically significant. This can be due to

- Only few patient were under ART in our study so the data can be too low to calculate statistical significance.

- Since it was the cross sectional studies we were not able place the events properly i.e. HIV transmission between partners have occurred before initiation of ART.

Anal sex and sex during menstruation

The practise of anal sex and sex during menstruation were statistically significant in the seroconcordant group which is similar to the findings observed in other studies. [102][106]

Condom usage

The proportion of condom usage was significantly high in serodiscordant groups as compared to the seroconcordant group. The protective effect of condom usage among serodiscordant couples have been demonstrated in various studies. [35][40] Similar findings have also been confirmed in the studies conducted by CDC, USA.[1]

Role of circumcision

Though the prevalence of circumcision was low (7%) this study population, it was significantly associated with serodiscordancy. Circumcision decreases the risk of achieving HIV infection in the heterosexual group up to 8 times compared to the uncircumcised population. This can be explained by a large number of Langerhans cells in the prepucial skin which act as the target for HIV virus. [46] Further it also reduces the likelihood of contracting STD, hence decreasing the chance of HIV

transmission. Inclusion of male circumcision into the current HIV prevention measure guidelines is warranted by the UNAIDS and the WHO in 2007(18).[46]

Previous venereal diseases

In this study 31% of the males and 11% of the females had a positive history of PVDs. The association of PVDs and the seroconcordant rates in males was statistical significant whereas it was not statistically significant in the females. However, there was a significant increase in the proportion of seroconcordance across the category of PVDs in the female population. A study conducted in Europe also shows association of PVDs with sexual transmission of HIV.[107] The statistical insignificance in the female population could be attributed to the following reasons

- Very less number of females had a positive history
- PVDs in the females are relatively asymptomatic
- Social stigma more predominant among the female population
- Low educational status leading to unawareness among them

Sexually transmitted infections and HIV transmission

40 males had sexually transmitted infections at the time of clinical examination. Among them 33 belonged to HIV seroconcordance group and the remaining were HIV serodiscordant. Among that 9 of them had mixed venereal diseases of which 8(88%) were HIV seroconcordant while 1(12%)

males were HIV serodiscordant. Genital ulcer disease was the commonest STI noted. Among the sexually transmitted infections, genital ulceration is associated with maximum seroconcordance rates. This is evidenced in various studies. [108-112]

Among the 39 females who had sexually transmitted infections, 10 females had multiple venereal diseases. Among them,9 belong to HIV positive seroconcordant group while 1 belong to HIV seropositive discordant group. Bacterial vaginosis was found to be the most common sexually transmitted infection (STI) in the female subjects. The presence of STI in both males and females were significantly associated with HIV transmission.

Conclusion

Conclusion

Majority of the couples in this study were HIV positive seroconcordant (65%) and the remaining 35% were serodiscordant.

On analysing the epidemiological characters of the study population we arrived at the following conclusions namely:

- Majority (75%) of the population were within the age group of 25-45 years. They were mostly urban inhabitants (68%) with low educational status and belonged to low socioeconomic strata.
- High risk behaviours such as contacts with commercial sex workers was more prevalent among the male population (84%) and few(9%) had history of contacts with homosexuals.
- Most of the index cases were male (92%) and the commonest reason for HIV screening was other departmental referrals (68%) and the commonest mode of acquisition of HIV was through heterosexual contacts (90%).

On analysing the various risk factors and their role in HIV transmission we concluded that:

- The presence of sexually transmitted infections in either the index case or their partners was significantly associated with HIV transmission. Among the sexually transmitted infections, genital ulcer disease had the maximum risk (>90%) of HIV transmission.

- The practise of anal intercourse, sex during menstruation and previous venereal diseases in males were also significantly associated with HIV transmission.
- Condom usage and circumcision had a significant role in decreasing the transmission of HIV among couples.
- Other risk factors such as duration of marital contact and number of sexual exposure per week were not significantly associated with HIV transmission.
- Previous venereal diseases in females and ART therapy had no significant role in HIV transmission.
- Most common sexually transmitted infection among the males were genital ulcer diseases while among female it was bacterial vaginosis.

In summary the univariate analysis of the above risk factors suggested that HIV concordance was significantly associated with presence of sexually transmitted infections, previous venereal diseases in males, anal intercourse, and sexual contact during menstruation, avoidance of condom during sexual act and lack of circumcision. Duration and frequency of sexual contact with partner, previous venereal diseases in females and ART were found not to influence the transmission of HIV.

Based on this study, it is necessary that the partners of HIV infected persons are identified, counselled and offered HIV testing since they are at the highest risk of acquiring HIV infection. Further high rates of co-occurring STI

in people living with HIV/AIDS will impede the efforts taken to prevent HIV transmission. Therefore aggressive behavioral interventions that include STI screening and treatment of all sexually active HIV-infected persons becomes imperative.

Limitations of the study

1. Since it was a cross sectional study there was difficulty in determining the sequence of events. For example, some of the potential risk factors for concordance may not have occurred before the partner was infected with HIV.
2. Bias is another problem in this study. Data referring to previous years may be affected by recall bias, and information on sexual practices and drug use may additionally be affected by reporting bias.
3. The study had a small sample size and hence statistical analysis may not be conclusive in some of the risk factors in relation to HIV concordance.

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Proforma

PROFOMA :

Serial No. :

STD OP No :

Name :

Sex :

Age :

- ☐ 18-25
- ☐ 26-35
- ☐ 36-45
- ☐ ≥46

Address :

- ☐ *Urban*
- ☐ Rural

Occupation :

- ☐ Private Employee
- ☐ Government Employee
- ☐ Self Employee
- ☐ Unemployed

Monthly Income:

- ☐ <1000
- ☐ 1000-4000
- ☐ >4000

Education Status:

- ☐ Illiterate
- ☐ <5th
- ☐ 6th – 12th
- ☐ Graduate

Sexual History:

Married since
- ☐ < 5years
- ☐ 5-10 years
- ☐ 11-15 years
- ☐ > 15 years

Premarital Contact yes No

If yes
- ☐ Commercial sexworker
- ☐ Homosexual
- ☐ transgender
- ☐ Known person

Extra marital contact Yes No

If yes
- ☐ commercial sexworker
- ☐ Homosexual
- ☐ Transgender
- ☐ Known person

Number of sexual contact with partner / week
- ☐ ≤1
- ☐ 2-3
- ☐ ≥4

Have practiced anal sex with partner
- ☐ Never
- ☐ Ever

Have practiced oral sex with partner
- ☐ Never
- ☐ Ever

Condom usage with partner

- ☐ Always
- ☐ Occasionally
- ☐ Never

Circumcision done (Male) Yes No

Sex during menstruation Yes No

Contraceptive followed

- ☐ Oral
- ☐ IUD
- ☐ Shield
- ☐ Condom
- ☐ No contraceptive

Previous history of sexually transmitted infection Yes No

If yes

- ☐ Genital ulcer
- ☐ Genital discharge
- ☐ Others

Presenting complaints

Genital ulcer

Genital discharge

Duration

Others if specify

H/O Itching over genitalia

H/O swelling in inguinal region

H/O burning micturition

H/O lower abdominal pain

H/O Dyspareunia

H/O oral lesion

IN FEMALES

Menstrual H/O

Obstetric H/O

Past history

TB, BA, any major illness.

H/O blood transfusions and any major surgeries.

Personal history

H/O alcohol intake

H/O smoking

H/O IV Drug abuse

General Examination

Pallor, Icterus, Cyanosis, Clubbing ,lymphadenopathy

Pulse rate, blood pressure

CVS

RS

CNS

P/A

Skin and mucous membrane

Genital Examination

Examination Inguinal lymphnode

External genitalia for any genital lesion

IN FEMALES

Speculum examination

Bi manual Examination

Master Chart

MASTER CHART

s.no	relation	Age	u/r	income	edu	HIV status	reason HIV	ART	married since	high risk sexual behaviour	nos. sexual contact/week	anal sex	orals sex	condom usage	circumcission	sex during menses	sexual orientation	PVD	sti	c/d
1	H	3	U	2	3	R	2	N	4	1,2	1	N	N	1	N	N	B	0	1,3	D
1	W	3			3	NR	4			N								0	0	
2	H	3	R	2	2	R	2	N	3	1,2	3	N	N	1	N	N	H	0	0	C
2	W	2			1	R	4			N								3	0	
3	H	2	U	2	3	R	2	N	2	1	2	Y	N	1	N	Y	H	1	3	C
3	W	2			3	R	4			N								0	8	
4	H	4	U	2	3	R	2	Y	4	1,2	2	N	N	1	N	Y	B	0	3,4	C
4	W	4			2	R	4			N								0	3,7	
5	H	4	U	2	4	R	5	N	4	1,3	2	N	N	1	N	N	H	0	0	C
5	W	4			3	R	4			N								0	0	
6	H	3	U	2	3	R	5	N	3	D	2	N	N	2	N	N	H	0	0	D
6	W	3			2	NR	4			N								0	0	
7	H	3	R	2	3	NR	4		2	N	1	N	N	1	Y	N	H	0	0	D
7	W	3			2	R	5	Y		1								0	0	
8	H	2	U	1	3	NR	4	N	1	N	2	N	N	1	N	N	H	0	0	D
8	W	2			1	R	5			1								0	0	
9	H	3	R	1	2	R	5	N	3	1	2	N	N	1	Y	N	H	0	0	D
9	W	3			1	NR	4			N								0	0	
10	H	3	U	2	3	R	5	N	2	1	2	N	N	1	N	N	H	0	0	D
10	W	3			3	NR	4			N								0	0	
11	H	2	R	1	3	R	5	Y	1	1	2	N	N	2	N	N	H	0	0	D
11	W	1			1	NR	4			N								0	0	
12	H	3	U	2	3	R	5	Y	4	1	2	N	N	2	N	N	H	0	0	D
12	W	3			3	NR	4			N								0	0	
13	H	3	U	2	3	R	5	N	4	1	2	Y	N	1	N	Y	H	0	0	C
13	W	3			3	R	4			N								0	10	
14	H	3	R	1	2	R	1	N	4	1,3	2	Y	N	1	N	Y	H	0	5	C
14	W	3			1	R	4			N								0	0	
15	H	3	U	2	3	R	2	N	3	1	2	Y	N	1	N	Y	H	0	2	C
15	W	3			3	R	4			N								0	0	

16	H	3	R	1	1	R	5	N	3	1,3	3	N	N	1	N	N	H	0	5	C
16	W	3			1	R	4			N								0	10	
17	H	3	U	2	2	R	5	N	4	1,2	2	Y	N	2	N	N	B	0	0	C
17	W	3			1	R	4			N								0	7	
18	H	3	U	2	3	R	1	N	1	1	2	N	N	1	N	N	H	0	6	D
18	W	3			3	NR	4			N								0	0	
19	H	2	U	2	3	R	5	N	2	1	2	N	N	2	N	N	H	0	0	D
19	W	1			3	NR	4			N								0	0	
20	H	3	U	2	2	R	5	N	2	1	1	N	N	2	N	N	H	0	0	D
20	W	3			1	NR	4			N								0	0	
21	H	3	U	2	3	R	5	N	2	1	2	N	N	1	N	N	H	0	0	D
21	W	3			3	NR	4			N								0	0	
22	H	3	U	2	3	R	1	N	3	1,2	2	N	N	2	N	N	H	1	0	D
22	W	3			3	NR	4			N								0	0	
23	H	2	U	2	3	NR	4	N	4	N	2	N	N	1	N	N	H	0	1	D
23	W	2			3	R	2			3								3	1	
24	H	3	R	2	3	R	2	N	3	2	1	N	N	2	N	N	H	0	1,3	D
24	W	3			3	NR	4			N								0	0	
25	H	3	U	2	4	R	5	N	1	D	2	N	N	2	N	N	H	0	0	D
25	W	2			4	NR	4			N								0	0	
26	H	3	R	1	2	R	5	N	2	1	2	N	N	2	N	N	H	0	0	D
26	W	2			1	NR	4			N								0	0	
27	H	2	U	2	3	R	5	N	3	2	2	N	N	2	N	N	B	2	6	D
27	W	2			2	NR	4			N								0	0	
28	H	4	U	2	3	R	5	N	3	1	2	N	N	1	Y	N	H	0	0	D
28	W	4			2	NR	4			N								0	0	
29	H	5	U	2	3	R	5	N	4	1	2	N	N	2	N	N	H	0	0	C
29	W	4			3	R	4			N								0	0	
30	H	5	U	2	2	NR	4	N	2	N	2	N	N	1	N	N	H	0	0	D
30	W	4			1	R	5			3								0	0	
31	H	4	U	2	3	R	2	N	3	1	2	Y	N	U	N	Y	H	1	0	C
31	W	4			3	R	4			N								0	8	
32	H	3	U	2	3	R	5	N	2	1,3	2	N	N	1	N	Y	H	0	0	C
32	W	3			1	R	4			N								0	8,9,10	
33	H	4	R	2	1	R	5	N	4	3	2	N	N	1	N	Y	H	0	5	C

33	W	3			1	R	4			N								0	10	
34	H	4	U	2	3	R	5	N	4	1	2	Y	N	1	N	Y	H	0	0	C
34	W	3			3	R	4			N								0	10	
35	H	2	U	2	3	R	5	N	4	1	2	N	N	1	N	N	H	0	0	C
35	W	2			3	R	4			N								0	10	
36	H	2	R	1	3	R	5	N	3	1	3	N	N	2	N	Y	H	0	6	C
36	W	2			3	R	4			N								0	0	
37	H	5	U	3	4	R	5	Y	4	1	1	N	N	2	N	N	H	0	6	D
37	W	4			4	NR	4			N								0	0	
38	H	1	R	2	2	R	1	N	1	1	2	N	N	2	N	N	H	0	7,8	D
38	W	1			1	NR	4			N								0	0	
39	H	3	U	1	3	R	5	N	3	3	2	Y	N	1	N	Y	H	0	5	C
39	W	3			3	R	4			N								0	8	
40	H	4	U	1	3	R	5	Y	3	1	2	Y	N	1	N	N	H	1	5	C
40	W	3			3	R	4			N								0	7	
41	H	2	R	1	1	R	5	D	2	1	2	Y	N	1	N	Y	H	1	6	C
41	W	2			1	R	4			N								0	7,8	
42	H	2	U	2	3	R	4	N	2	1	3	Y	N	1	Y	N	H	1	0	C
42	W	2			2	R	3			N								0	0	
43	H	2	U	2	3	R	5	N	2	1	2	Y	N	1	N	Y	H	2	0	C
43	W	2			3	R	4			N								0	8,9,10	
44	H	3	R	1	1	NR	4		2	1	2	N	N	1	N	N	H	0	0	D
44	W	2			1	R	2	N		N								0	11	
45	H	5	R	1	1	R	5	N	4	1	2	N	N	1	N	Y	H	0	0	C
45	W	4			1	R	4			N								0	0	
46	H	4	U	2	1	R	5	N	4	1	2	y	N	1	N	N	H	0	5	C
46	W	3			1	R	4			N								0	0	
47	H	3	U	2	3	R	5	N	4	1	2	Y	N	1	N	N	H	0	4	C
47	W	2			3	R	4			N								0	0	
48	H	2	U	1	3	R	2	N	1	1	2	Y	N	1	N	Y	H	0	4	C
48	W	2			3	R	4			N								0	0	
49	H	3	R	2	3	R	2	N	2	1	2	Y	N	1	N	Y	H	1	4	C
49	W	3			2	R	4			N								0	0	
50	H	4	U	2	3	R	5	Y	3	1	2	N	N	1	N	N	H	4	0	C
50	W	2			3	R	4			N								0	0	

51	H	2	U	1	3	R	1	N	1	1	1	N	N	2	N	N	B	0	5	D
51	W	2			2	NR	4			N								0	0	
52	H	5	U	2	1	NR	4		4	1	1	N	N	1	N	N	H	0	0	D
52	W	4			1	R	5	N		N								0	8	
53	H	4	U	2	3	R	5	N	4	1	2	N	N	1	N	N	H	0	5	C
53	W	3			2	R	4			N								3	0	
54	H	2	R	2	3	R	5	N	3	1	3	Y	N	1	N	N	H	0	0	C
54	W	2			3	R	4			N								0	0	
55	H	2	R	2	3	R	2	N	1	1	2	Y	N	1	N	Y	H	0	3	C
55	W	2			1	R	4			N								0	0	
56	H	2	U	1	3	R	2	N	2	1	2	Y	N	1	N	Y	H	1	1,4	C
56	W	2			3	R	4			N								0	1	
57	H	3	U	1	1	R	5	N	4	1	2	N	N	1	N	N	H	0	0	D
57	W	3			1	NR	4			N								0	0	
58	H	4	U	2	3	R	2	N	4	1	3	Y	N	1	N	N	H	0	4,6	C
58	W	3			3	R	4			N								0	0	
59	H	3	U	2	2	R	5	N	2	3	2	Y	N	2	N	Y	H	1	0	C
59	W	3			1	R	4			N								0	0	
60	H	4	U	1	2	R	1	N	4	3	2	Y	N	1	N	Y	H	0	13	C
60	W	3			1	R	4			N								0	1,9	
61	H	5	U	2	3	R	5	N	3	1	2	Y	N	1	N	Y	H	0	0	C
61	W	3			3	R	4			N								0	8	
62	H	3	U	2	2	R	5	N	2	1	1	Y	N	1	N	Y	H	0	5	C
62	W	2			2	R	4			N								0	7	
63	H	2	R	1	2	R	2	N	1	1	2	Y	N	1	N	N	B	0	2	C
63	W	1			1	R	4			N								0	2,7	
64	H	3	U	1	3	R	5	Y	2	1	2	N	N	1	N	N	H	0	0	C
64	W	3			1	R	4			N								0	4	
65	H	4	U	2	3	R	2	N	4	3,2	3	Y	N	1	N	N	B	1	1,4	C
65	W	3			3	R	4			N								0	1	
66	H	3	R	2	3	R	2	N	3	1	2	Y	N	1	N	N	H	0	2	C
66	W	2			1	R	4			N								0	0	
67	H	4	U	2	2	R	5	N	4	1	2	Y	N	1	N	Y	H	0	0	C
67	W	3			1	R	4			N								0	8	
68	H	3	R	1	1	R	5	N	3	1	2	Y	N	U	N	Y	H	0	0	C

68	W	2			1	R	4			N								0	4	
69	H	4	U	2	3	R	5	N	4	1	1	Y	N	U	N	Y	H	1	0	C
69	W	3			1	R	4			N								3	0	
70	H	2	U	2	4	R	5	Y	1	N	2	N	N	2	N	N	H	0	0	C
70	W	2			4	R	4			N								0	0	
71	H	3	U	2	2	R	5	N	3	1	2	Y	N	1	N	Y	H	1	0	C
71	W	3			1	R	4			N								0	4	
72	H	2	U	2	2	R	5	N	2	1	2	Y	N	1	N	Y	H	0	0	C
72	W	2			2	R	4			N								0	9,8	
73	H	3	R	1	1	R	5	N	4	1	2	Y	N	1	N	N	H	0	5	C
73	W	2			1	R	4			N								0	10	
74	H	3	U	2	3	R	5	N	3	1	2	N	N	1	N	Y	H	0	0	C
74	W	2			3	R	4			N								0	8,9	
75	H	3	R	2	2	R	5	N	1	1	2	Y	N	1	N	Y	H	0	0	C
75	W	3			2	R	4			N								0	4	
76	H	2	U	1	3	R	5	N	1	1	2	N	N	1	N	N	H	0	0	C
76	W	1			3	R	4			N								0	8,9	
77	H	2	U	2	3	R	4	N	1	1	2	Y	N	1	N	Y	H	0	0	C
77	W	1			3	R	3			N								0	0	
78	H	2	U	2	2	R	4	N	1	1	3	Y	N	1	N	Y	H	1	1	C
78	W	1			3	R	3			N								1	1	
79	H	2	R	2	1	R	5	N	2	1	3	Y	N	1	N	N	H	1	1	C
79	W	1			1	R	4			N								0	1	
80	H	3	U	2	3	R	5	Y	3	1	2	N	N	2	N	N	H	1	0	D
80	W	2			3	NR	4			N								0	0	
81	H	3	U	2	3	R	1	N	4	1	2	N	N	2	N	N	H	0	0	D
81	W	2			1	NR	4			N								0	0	
82	H	2	R	1	1	R	5	N	2	3	3	N	N	1	N	Y	H	0	0	C
82	W	2			1	R	4			N								0	0	
83	H	2	U	2	1	R	1	N	1	1	3	N	N	1	Y	N	H	0	0	D
83	W	1			3	NR	4			N								0	0	
84	H	2	R	1	2	R	5	D	1	1	2	Y	N	1	N	Y	H	1	0	C
84	W	1			1	R	4			N								0	0	
85	H	3	U	1	2	R	5	N	2	1	2	N	N	1	N	N	H	1	3	C
85	W	2			1	R	4			N								0	0	

86	H	3	R	1	3	NR	5	N	3	1	1	N	N	1	N	N	B	0	3	D
86	W	3			2	R	4			N								0	0	
87	H	4	R	1	1	R	5	N	4	1	1	N	N	1	N	N	H	0	0	C
87	W	4			1	R	4			N								0	7	
88	H	2	U	2	3	R	2	N	2	1	3	Y	N	1	N	Y	H	0	1,4	C
88	W	2			2	R	4			N								0	1	
89	H	2	U	2	1	R	1	N	1	1	1	N	N	1	Y	N	H	0	0	D
89	W	2			1	NR	4			N								0	0	
90	H	4	U	1	3	R	5	Y	4	1	2	N	N	1	N	N	H	1	2	C
90	W	3			1	R	4			N								0	0	
91	H	4	R	2	2	R	5	N	2	3	2	N	N	1	N	N	H	0	2	C
91	W	3			2	R	4			N								0	0	
92	H	3	U	1	3	R	5	Y	2	1	2	N	N	2	Y	Y	H	0	0	D
92	W	2			3	NR	4			N								0	0	
93	H	3	U	2	2	R	5	N	2	1	2	N	N	1	N	N	H	0	0	D
93	W	2			2	NR	4			3								0	0	
94	H	3	U	2	3	R	5	N	1	1	2	Y	N	2	N	N	H	0	0	D
94	W	2			3	NR	4			N								0	0	
95	H	3	U	1	2	R	2	N	1	1	2	Y	N	1	N	Y	H	0	2	C
95	W	2			1	R	4			N								0	8	
96	H	4	R	1	1	R	5	N	2	3	2	N	N	1	N	Y	H	0	0	C
96	W	3			1	R	4			N								0	0	
97	H	3	U	2	3	R	5	N	2	1	2	N	N	1	N	N	H	0	6	C
97	W	1			2	R	4			N								0	0	
98	H	3	R	2	3	NR	4	N	2	3	3	N	N	2	N	N	H	0	7	D
98	W	1			3	R	5			3								0	7	
99	H	2	R	1	2	R	1	N	2	1	2	N	N	1	N	N	H	0	0	C
99	W	1			1	R	4			N								0	0	
100	H	3	R	1	2	R	5	N	2	1	2	N	N	1	N	y	H	0	3	C
100	W	1			2	R	4			N								0	9	

H=husband
W=wife

Age
1 18-25
2 26-35
3 36-45
4 46-55
5 >=56

Address
U -urban
r-rural

Monthly income
1- <2000
2-2000 to 5000
3->5000

education status
1 - illiterate
2 - < 5th
3 - 6th to 12th
4 - graduate

Married since
<5 years
5-10years
11-15 years
>15 years

Condom
1 never
2 occasiona
3 always

Serostatus
C-Seroconcordance
D -Serodiscordance

sex during menses
0=no
1=yes

anal sex
0= no
1=yes

ART=anti retroviral therapy
0=not on ART
1=on ART

high risk sexual behaviour
1 - commercial sex work
2 - homosexual
3 - known person

reason for HIV screening
1 - high risk behaviour
2 - presence of STIs
3 - maternal screening
4 - spouse HIV positive
5 - refer from other department

PVDs
1 - genital ulcer
2 - urethritis
3 - vaginal discharge
4 - balanophosthitis

STIs
1 - VDRL reactivity
2 - herpes
3 - anogenital wart
4 - nonspecific genital ulceration
5 - non specific urethritis
6 - balanoposthitis
7 - vulvovaginal candidiasis
8 - bacterial vaginosis
9 - trichomonas vaginalis
10 - cervicitis
11 - bartholin abscess

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3

Telephone No: 04425305301
Fax : 04425363970

CERTIFICATE OF APPROVAL

To
Dr. K. Radha Raja Prabha
PG in MDDVL
Madras Medical College, Chennai -3.

Dear Dr. K. Radha raja prabha

The Institutional Ethics Committee of Madras Medical College reviewed and discussed your application for approval of the proposal entitled " A clinicoepidemiological study of HIV seroconcordant Vs serodiscordant couples " No. 10102011.

The following members of Ethics Committee were present in the meeting held on 20.10.2011 conducted at Madras Medical College, Chennai -3.

1.	Prof. S.K. Rajan, MD	-- Chairperson
2.	Prof. A. Sundaram, MD Vice Principal , Madras Medical College, Chennai -3	-- Member Secretary
3.	Prof R. Nandhini, MD Director, Institute of Pharmacology, MMC, Ch-3	-- Member
4.	Prof. C. Rajendiran, MD Director , Institute of Internal Medicine, MMC, Ch-3	-- Member
5.	Thiru. A. Ulaganathan Administrative Officer, MMC, Chennai -3	-- Layperson
6.	Thiru. S. Govindasamy . BA.BL	-- Lawyer
7 .	Tmt. Arnold Soulina MA	-- Social Scientist
8.	Prof. Shanta Ravishankar Prof of Neuropathology, M M C, Chennai -3	-- Member

We approve the proposal to be conducted in its presented form

Sd /. Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information / informed consent and asks to be provided a copy of the final report

Member Secretary, Ethics Committee